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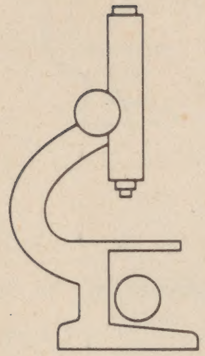

TUBERCULOSIS

I. Diagnosis

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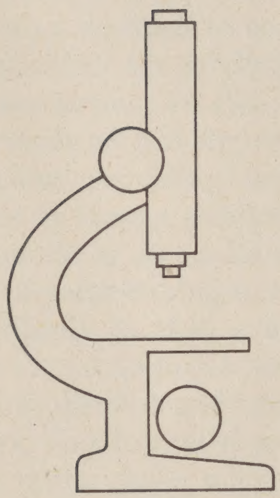
1945

X-RAY. MASS RADIOLOGY

MINIMAL PULMONARY TUBERCULOSIS

BRONCHIOGENIC CARCINOMAS



X-RAY. MASS RADIOLOGY

OUTLOOK FOR TUBERCULOSIS CONTROL IN THE CIVILIAN POPULATION[1]

THOMAS PARRAN[2]

The present outlook for the conquest of tuberculosis is indeed encouraging. But those of us who have fought the long fight together so many years know from experience that the final struggle will not be easy. For centuries before Koch's discovery of the tubercle bacillus, the White Plague ravaged our civilization without let or hindrance. Aided by a rapidly rising standard of living, the health forces of the nation (with strong prodding from the National Tuberculosis Association) prosecuted a successful first campaign. The death rate from tuberculosis in the United States was halved and halved again between 1900 and 1940.

Tuberculosis control was one of the first activities in public health in which the coöperation of the public and the profession led to substantial advances. This was the first instance in which we undertook to control a disease, not by specific immunization or quarantine, but essentially by the power of public education.

Our early successes however were destined to encounter stubborn resistance. There are many reasons to account for the leveling off of accomplishment and the lack of progress in the last ten years. In 1937, Wade Hampton Frost considered that in the country as a whole we had tipped the biological scales against the survival of the tubercle bacillus, providing control were maintained at the same level and that no decrease in human resistance to the disease occurred. To put it another way, tuberculosis in an unchanging society and subject to existing controls was no longer self-perpetuating and would eventually disappear. Many lives would be lost needlessly in that evolutionary process, however. Existing control measures were bound to prove less effective as the disease retreated into strongholds less easy to discover and breach. Indeed, it is a common experience in public health work that frontal attack on a wide-spread disease produces dramatic results in the initial phase, followed by a lag as the volume of infection diminishes.

As we view public health developments broadly, we see that we make progress —not evenly all along the line, against all diseases and conditions, nor continuously against a single disease, but because of some development in science, stirring the public interest, we are enabled to push ahead against one or another of the killers.

The development of diphtheria toxoid made it possible for us substantially to eradicate that disease. Recently we have seen nation-wide interest in the control of the venereal diseases and a substantial national program is now underway with gratifying results in the control of syphilis and gonorrhoea.

[1] Presented in the symposium on *Tuberculosis and War* at a joint session of the Medical and Public Health Sections at the 40th annual meeting of the National Tuberculosis Association, Chicago, Illinois, May 12, 1944.

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Tuberculosis now comes to the fore again because scientific advances have awakened public interest. Recent technical developments make it possible to find cases cheaply and to find them early. The war, which has threatened the stability of our civilization, with consequent lowering of resistance to the disease, has directed renewed attention to tuberculosis control.

The stage is set, then, for a coördinated attack with the objective of eradicating—not merely controlling—tuberculosis. This is more than an altruistic dream; it is an urgent necessity, a practical goal.

WAR AND TUBERCULOSIS

Long wars accompanied by privation always have resulted in appalling increases in tuberculosis. In past centuries, this fact was masked by the immediately apparent catastrophe of acute epidemics. It remained for the World War of 1914–1918 to reveal tuberculosis as a major war problem. By 1917, the French Army had returned 150,000 tuberculous soldiers to civilian life. Thousands of exchanged prisoners of war had acquired the disease and were returning to France. All European nations, both neutral and combatant, experienced a rise in tuberculosis mortality varying from 10 to 20 per cent. Colonel Esmond Long has recently made the conservative estimate that tuberculosis mortality rose 15 per cent in all Europe for three years, "which would credit the war with about 200,000 tuberculosis deaths."

History has repeated itself tragically in this war, and with a ferocity inspired by the policy of the Germans to exterminate large groups in the conquered nations by slow death. It is known that tuberculosis is raging with epidemic force in conquered Europe to-day. In France, Professor André Mayer has reported that tuberculosis is epidemic and that, because of food shortages, a diagnosis of tuberculosis is almost a death sentence. Bigwood has reported a comparable situation in Belgium. Even Great Britain has experienced a 13 per cent increase in tuberculosis mortality since the war began.

Crowding, fatigue, malnutrition, increased exposure, mass migrations of population—all these favor the spread of tuberculosis in wartime. Although we cannot yet point to a nation-wide increase in tuberculosis mortality in the United States, indications in certain parts of the country are that such a rise will soon become apparent.

THE PUBLIC HEALTH SERVICE WAR PROGRAM

Recognizing this potential threat the Public Health Service has sought a means to avert it. Prior to the outbreak of war in 1939, we had become interested in the possibilities of the small-film X-ray as a public health method for mass case-finding. Intensive coöperation studies carried on for several years resulted in improvement of the technique to the point where its effectiveness could be clearly demonstrated. The time seemed ripe, therefore, immediately after Pearl Harbor to put this new tool to work with a view to checking the spread of tuberculosis in the most vulnerable group of civilians, namely, the workers in war industries.

Accordingly, we used a part of our Emergency Health and Sanitation appropriation to establish a small tuberculosis control office and to put into the field several mobile X-ray units to conduct case-finding surveys in war industries. We had also a responsibility to the greatly expanded United States Coast Guard and routine X-ray examinations were instituted at its training stations. As you know, both the Navy and the Army made the inclusion of chest X-ray examinations obligatory for all recruits.

In the two and one-half years of operation, our wartime tuberculosis program has more than proved its worth. In fact, "We started something." We have continually improved our performance with the small-film technique, so much so that a single unit can take and process, on the average, 500 films in an eight-hour day. With a double staff, the machine could work two shifts and complete 1,000 examinations in twenty-four hours. This past year, one of our medical officers, Dr. Russell H. Morgan, formerly of the University of Chicago, has perfected a phototimer for use with the fluorograph. This device doubles production and improves quality of the picture.

At no time have we had more than eight units in the field and because of budgetary limitations we have never been able to meet all the requests for this service. During the coming fiscal year, 1945, we shall be able to expand this service moderately. In fact, the Public Health Service has been somewhat like the Dutch boy who took the initiative and plugged the hole in the dike with his hand until help arrived.

Despite the limitations, we have these accomplishments to report. Nearly three-quarters of a million persons—war workers and their families—have been examined. More than one in every 100 (1.3 per cent) have shown evidence of reinfection tuberculosis. The great, the encouraging significance of these findings is that 62 per cent of the cases discovered in our surveys are in the minimal stage when recovery is almost certain with good care. Thirty-one per cent of the cases are moderately advanced; and 7 per cent far advanced. This is almost a complete reversal of past experience, when not more than 10 per cent of the patients coming to treatment for the first time were in the early stage of their disease.

During the past year, we have also been able to give a little help in consultant service to states desiring to strengthen their tuberculosis control work.

Our experience in these two years of war service has proved of value in shaping the final attack. We are under no illusion that the discovery of one, or a thousand, or a million cases of tuberculosis will alter the course of the disease in this country, unless the cases discovered receive needed care to prevent further spread.

THE BURDEN OF TUBERCULOSIS IN THE UNITED STATES

No stratum of society is free of tuberculosis. No family is truly safe as long as the disease smolders in any sector of the community. On the average, nearly 60,000 persons die of tuberculosis in this country every year. About half of them are men and women in the most productive years of life. Tuberculosis

has been listed seventh among the important causes of death in the general population for a number of years; it is the *first* cause, except accidents, among young adults, fifteen to thirty-five. In the colored population, it is the *second* cause of death, all ages, exceeded only by heart disease.

Indeed, American Negroes and Indians and Americans of Spanish-speaking races bear from three to six times their proportionate burden of tuberculosis. Among Negroes twenty to thirty-four years of age, one in every 3 deaths is due to tuberculosis; while among their white neighbors of the same ages, the ratio is one in 6. To-day the tuberculosis mortality in the colored population stands at a higher rate than among whites in 1919!

The interrelationship of poverty, ignorance and disease is nowhere more clearly demonstrated than in the prevalence of tuberculosis. From the earliest studies of sickness and occupation, we have known that this disease is an important cause of death among industrial workers. In the United States, tuberculosis kills seven times more frequently among unskilled workers than among professional groups.

The disease works its greatest havoc among low income groups. Despite increased employment in wartime, higher wages in some occupations and an all-time high national income, the economic stratification of the nation has not changed. There are still low income groups. The tremendous expansion of industry, together with increased employment of women, older men and under-draft-age boys, has accelerated the exposure to tuberculosis.

The colored population is at the bottom of the economic ladder. Their homes, now as before the war, are the most miserable; their daily diet most out of balance; and their ability to purchase health service and other necessities of life is the least. No plan to rid American life of tuberculosis can overlook this close alliance of poverty and disease.

The war has also been accompanied by great shifts in the industrial population, as war industries have blossomed in areas ill-prepared to deal with increased health problems. Many war workers who are not residents of the communities where they are now employed have broken down with tuberculosis. They cannot always receive sanatorium care at public expense because they are not eligible under local residency laws. Many cannot be returned to their original homes for care, because there they have lost residency. It is no wonder that state health departments are greatly concerned about the nonresident war workers and their families who develop tuberculosis.

In 1938, it was estimated that the United States maintains a tuberculous population of 1,500,000. If we apply to the total population the percentage of cases found in our X-ray surveys among war workers and their families, we arrive at about the same figure. The notable difference is that, in 1938, the estimate was based on deaths; to-day our findings are represented by the living—known patients who can be helped, the vast majority of them saved from premature death.

In the large group of known cases revealed by mass X-ray surveys, there are over 100,000 young men and women rejected at the examining and induction

stations of the armed forces. The Public Health Service has coöperated with the Army, Navy and the Selective Service System in bringing those rejected for tuberculosis to the attention of their state health departments for follow-up and treatment. The results to date have not been good, largely because available resources in personnel and facilities are not adequate for the task.

Already many veterans of World War II have been discharged because of tuberculosis. Although these men are eligible for care by the Veterans Administration, about one-third of those who enter the hospitals leave in a few weeks' time and return to their home communities, where they become a public health problem.

JOINT RESOURCES IN A JOINT ENTERPRISE

Now that it is possible to raise the visibility of our tuberculosis problem in every part of the country, we have no reason for delaying a concentrated attack. Beginning in true public health fashion where there is the greatest opportunity for life-saving, we should direct all available resources in a determined, systematic and continuing drive against the tubercle bacillus until we have attained a final victory.

The modern concept of public health control is as simple as it is sensible: Find all cases early; treat all patients, continuously and competently. Underlying both is education. These have been the guiding principles of the national venereal disease control program.

A comparable job needs to be done in tuberculosis control, but only if public and private agencies work side by side in a joint enterprise, utilizing joint resources, may success be expected.

As I see it, a national program of tuberculosis control is necessary. It can be developed from the foundations laid by the National Tuberculosis Association, the Public Health Service and the state health authorities.

The need for nation-wide, coördinated effort is obvious. Not more than half of the 48 states now have full-time medical officers in their health departments to conduct an efficient, basic program of case-finding and follow-up. Not more than half have sufficient clinic facilities for the follow-up of ambulatory patients. Very few state health departments have efficient tuberculosis record systems, which are so essential in control procedures.

As we have seen, wartime migration has further emphasized the national character of the problem. Anticipated postwar migrations are sufficient reasons for immediate action to equalize the effort against tuberculosis geographically. The load is heaviest in the poorest states. But no matter how effective the control in a single state, its citizens are not safe until the citizens in all states receive comparable protection.

More research is needed, in at least three important fields. We have already seen the value of limited research in public health methods and equipment. It is reasonable to assume that further improvements can be made by intensified research in their field. Expanded research on chemotherapy in tuberculosis is indicated. It is difficult for us to realize that the prevention and cure of tubercu-

losis is still dependent upon the frailty of the bacillus and the relative strength of the patient's natural resistance. More research is needed to find, if possible, a specific cure. Finally, epidemiological research on a world-wide basis is essential if we are ultimately to conquer tuberculosis. This war has taught us that safety within our borders does not protect us from outside dangers; our defense against tuberculosis is intimately bound up with the defense made by other nations.

The tuberculosis problem has been whittled down to a measurable size. With measurable funds and effort, we can come to grips with it confidently, in the whole nation. We should not be satisfied with Frost's slightly favorable biological balance. Extermination should be our goal.

The finding of cases will create facilities for their care: hospital sanatoria, work colonies for the older patients with chronic disease, financial aid for the tuberculous bread-winner all are needed. The protection of the healthy population and the proper use of treatment facilities require the development of some system whereby these cases can be isolated in a humane way.

It is in the local communities, in the individual home, that tuberculosis occurs; it is there that the problems must be met. Local health agencies, official and voluntary, would coördinate all available community resources, working closely with local medical profession and welfare groups whose help will be needed to the fullest.

The importance of team-work among all responsible groups is accentuated by the shortage of sanatorium beds in many parts of the country, wartime restrictions on new construction and the even more acute shortage of medical, nursing and other personnel in hospitals, health services and private practice.

OBJECTIVES OF A PROGRAM TO ERADICATE TUBERCULOSIS

To achieve our final objective, our immediate aims must be definite and specific. The essentials of a good tuberculosis program can be summarized briefly:

1. X-ray examination for the entire population, concentrating first on the vulnerable groups and their family contacts. This does not exclude the use of pre-X-ray tuberculin testing among selected groups with low infection rates.
2. Follow-up of every case discovered in X-ray examinations, in order to insure clinical diagnosis and proper treatment. This would include supervision by physicians in private offices or clinics, assisted by public health nurses; sanatorium care, protective supervision after discharge and rehabilitation where indicated.
3. Periodic examination, including chest X-ray films, of persons with inactive disease.
4. Prompt treatment for active cases which can make a good recovery.
5. Strict isolation of open cases to prevent further spread of the disease.
6. Intensified health education activities among the general population, patients and their families.
7. Expanded research in tuberculosis and control methods.

Finally, all of us who so ardently desire to see tuberculosis banished from our land must recognize that this cannot be done unless some financial provision is made for the tuberculous bread-winner, who must leave his family without adequate resources if he, himself, is to give up his job after treatment. We know that sickness breeds poverty, as poverty breeds sickness. The path of the tuberculosis patient is like that of one lost in an Arctic storm; he travels in a vicious circle of poverty and disease. Somewhere the circle must be broken, and the path made straight and upward—to health and economic independence.

Only if we recognize tuberculosis in all its aspects as an unnecessary cause of suffering and death, and treat it medically, socially and economically, shall we be able to conquer it. The outlook for control is encouraging, the future bright with hope. But as tuberculosis is the people's problem, its solution depends on the people's active willing coöperation. Nineteen-hundred and forty-four may well be the "year of decision" which determines the fate of the tubercle bacillus in the United States. The American people now have the opportunity to decide whether tuberculosis shall continue a needless and costly burden on the nation, or shall be exterminated. I am confident that, with the leadership of the National Tuberculosis Association, the decision will be against our common enemy.

SUMMARY

The outlook for the conquest of tuberculosis in the United States is encouraging. Technical developments have made it possible to find cases cheaply and to find them early. The war, which has threatened the stability of our civilization, with consequent lowering of resistance to the disease, has awakened public interest in tuberculosis control.

The Public Health Service has taken steps to prevent a wartime rise in tuberculosis. Mobile small film X-ray units have conducted mass case-finding surveys among workers in war industries—the most vulnerable group in the population. Routine X-ray examinations were instituted at United States Coast Guard training stations. Both the Army and the Navy included chest X-ray films in their examinations of all recruits.

Nearly three-quarters of a million persons—war workers and their families—have been examined by the U. S. Public Health Service, more than one in every 100 (1.3 per cent) have shown evidence of reinfection tuberculosis. Sixty-two per cent of the cases discovered are in the minimal stage when recovery is almost certain with good care. Thirty-one per cent of the cases are moderately advanced and 7 per cent far advanced. This is almost a complete reversal of past experience, when not more than 10 per cent of the patients coming to treatment for the first time were in the early stage of their illness. The discovery of a million cases of tuberculosis will not alter the course of the disease in this country, however, unless the cases discovered receive needed care to prevent further spread.

Of nearly 60,000 persons who die of tuberculosis every year in the United States, about half are in the most productive years of life. Tuberculosis is seventh among

the important causes of death in the general population; first, except accidents, among young adults, fifteen to thirty-five; second among the colored population, all ages; and from third to sixth among Spanish, Indian and Negro races. In industry, tuberculosis kills seven times more frequently among unskilled workers than among professional groups. No plan to rid America of tuberculosis can overlook the close alliance of poverty and this disease.

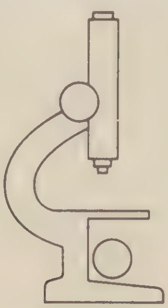
About 130,000 young men and women have been rejected at the examining and induction stations of the armed forces. The Public Health Service has coöperated with the armed forces in bringing these rejectees to the attention of their State Health Departments for follow-up and treatment. About one-third of the many tuberculous veterans of World War II who enter veterans' hospitals leave in a few weeks' time and return to their home communities, where they become a public health problem.

Now that we realize the tuberculosis problem in every part of the country, public and private agencies need to work side by side in a joint enterprise, utilizing joint resources, under the stimulus of a national program. The foundations for such a program have been laid by the National Tuberculosis Association, the Public Health Service and the State health authorities.

In a national program, the accepted pattern of Federal assistance to States would be applied under a specific authorization of funds by the Congress. State health authorities in turn would take the leadership in the establishment and support of tuberculosis control programs in local health departments. Local health agencies, official and voluntary, would coördinate all available community resources, working closely with local medical profession and welfare groups whose help will be needed to the fullest.

The essentials of an effective tuberculsosis program for the nation can be summarized briefly:

1. X-ray examination for the entire population.
2. Follow-up of every case discovered in X-ray examinations.
3. Periodic examination, including chest X-ray examination, of persons with inactive disease.
4. Prompt treatment for patients with active disease who can make a good recovery.
5. Strict isolation of open cases to prevent further spread of the disease.
6. Intensified health education activities among the general population, patients and their families.
7. Expanded research in tuberculosis and control methods.
8. Financial aid to the tuberculous bread-winner.



AN EVALUATION OF THE ROENTGEN METHODS USED IN MASS CHEST SURVEYS

IT IS generally recognized that the incidence of pulmonary tuberculosis might be effectively reduced if those individuals with active disease were isolated at the earliest possible moment. Since early isolation presupposes early detection and since the roentgen examination constitutes the most reliable method for the early diagnosis of pulmonary tuberculosis, it is evident that considerable progress in the control of this disease might be achieved if the population at large were examined roentgenographically at regular intervals. Until the early 1930's such a program was impractical due to the excessive cost of the roentgen methods then available. In recent years, however, this situation has been spectacularly changed by the development of the photofluorographic process in which a fluorescent image of the chest is photographed on films of reduced size (usually 4×5 inch, or 35 mm. film). Such films, when made in large numbers, are considerably less expensive to produce, process and handle than standard 14×17 inch roentgenograms. Recently, the roll paper process in which 14×17 inch roentgenograms are made on sensitized paper has been perfected and may also prove a useful method for the examination of large population groups.

The photofluorographic process has been used extensively in this country in the examination of inductees entering the armed services and of many thousands of civilians engaged in industry, and there is every reason to expect that the process will receive progressively wider application as time goes on. Before the outbreak of the current war, photofluorography was an established procedure in many foreign countries, particularly in Brazil and Scandinavia.

The diagnostic quality of photofluorographic and paper film is somewhat inferior to that of 14×17 inch roentgenograms and, as a result, many radiologists have become concerned lest the diagnostic error of these newer methods be high and thereby largely counteract their other advantages. In an effort to determine the relative merits of the various roentgen methods which are available for the examination of the chest (14×17 inch roentgenographic film, 4×5 inch photofluorographic film, 35 mm. photofluorographic film, 14×17 inch sensitized paper, and roentgenoscopy), clinical studies in which two or more of the methods were compared have been made by several investigators. The conclusions reached vary widely and seem to depend on the experience or inexperience, as the case may be, of the interpreter. Furthermore, many of these studies have not been carefully controlled from the viewpoint of selection of samples and statistical analysis and accordingly the overall picture tends to be confused.

A direct quantitative evaluation of the diagnostic quality of the various roentgen procedures may be made by a comprehensive investigation of the physical characteristics of the several methods. From such a study it is possible to list in unequivocal terms the relative detail with which roentgen images may be resolved by each method and to determine the smallest lesion which a given method is capable of recording. During the past two years such a study has been under way at the University of Chicago. An attempt has been made to correlate the various physical factors which

influence roentgenographic and roentgenoscopic quality so that the part played by each in the total effect may be correctly evaluated. Physiological considerations of viewing have also been included. Although this material will be presented in detail in a series of articles which will appear in forthcoming issues of this JOURNAL, it has been thought desirable to summarize here some of the preliminary findings of the study so far as they relate to the various roentgen methods used in the examination of the chest.

The resolving power of 14×17 inch roentgenograms is superior to that of all other roentgenographic materials. In order of merit below these films may be listed, 4×5 inch photofluorograms, when made with a stationary-focused grid; 14×17 inch sensitized paper; 35 mm. photofluorograms when made with a stationary-focused grid, and 4×5 inch photofluorograms, made without a grid; 35 mm. photofluorograms, made without a grid; and, finally, roentgenoscopy.

The low resolution provided by the roentgenoscopic method may be attributed to the low visual acuity of the eye when operating at the low intensity levels present under roentgenoscopic conditions. A grid improves the diagnostic quality of photofluorograms by reducing the amount of scattered radiation reaching the fluorescent screen, and thereby increasing the contrast of the roentgen images. Due to the high inherent contrast of 14×17 inch roentgenographic film, and the relatively short useful density range of 14×17 inch paper film, a grid is not useful when these materials are employed.

It must be realized that the above list represents conditions as of 1944, and undoubtedly it will require considerable revision from time to time in the years to come. Indeed, there is reason to expect that, before long, 4×5 inch photofluorograms and eventually 35 mm. photofluorograms will be equivalent to present-day 14×17 inch roentgenograms.

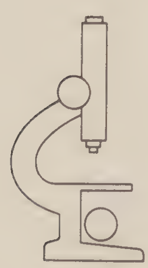
Although the foregoing discussion indicates the relative merits of the various roentgen procedures used in the examination of the chest, it does not provide any information as to the diagnostic error which may be expected from a given method in the detection of pulmonary tuberculosis. Physical studies reveal, however, that the smallest infiltrative lesion which may be detected by a competent observer using roentgenoscopy is between 0.5 and 1.0 cm. in diameter; smaller lesions, of course, can be detected with the other methods, with 14×17 inch roentgenograms being able to reproduce the smallest process. Since most significant lesions exceed 0.5 to 1.0 cm. in diameter, it is evident that all of the roentgen methods which are available for the examination of the chest should be capable of detecting the majority of tuberculous processes. One word of caution must be injected at this point, however. Since the resolution or detail with which a lesion may be seen varies widely in the different methods, one must not use the same diagnostic standards when interpreting the films produced by one method that are used when interpreting the films produced by another. For example, a particular tuberculous lesion will present considerably less detail in a 35 mm. film than that seen in a 14×17 inch roentgenogram. Indeed, if the lesion is small, its true significance may be easily overlooked if the roentgenologist unconsciously insists on the fulfillment of the criteria employed in the diagnosis of the larger film. A spectacular instance of this occurred recently when an acquaintance of the writer was asked to test his skill in interpreting 35 mm. photofluorograms. Fourteen by seventeen inch and 35 mm. films of several hundred individuals, of whom approximately 20 per cent were known to have minimal pulmonary tuberculosis, were submitted to this well known radiologist who until this time had read relatively few small films. The results of the test were at first highly disconcerting because a considerable number of cases called "positive" from the 14×17 inch films were called "negative" from the 35 mm. films. For-

tunately, however, the radiologist did not stop here but wisely reviewed the two series of films, comparing each 35 mm. photofluorogram with each 14×17 inch roentgenogram. In this way, he was able to establish for himself the diagnostic criteria which should be used in the interpretation of small films. After this educational program, another comparative series of 35 mm. photofluorograms and 14×17 inch roentgenograms was submitted to him for interpretation. The diagnostic error in reading the small films this time was of a much lower order.

The foregoing is a forceful demonstration that an ability to correctly diagnose the films produced by one roentgenographic method does not presuppose an equal ability to interpret the films produced by another. First, it is necessary for one to establish for himself the diagnostic criteria which are more or less peculiar to the roentgenograms made by a particular method. Such education may be accomplished in at least two ways. In one, perspective may be gained by the examination of many thousands of films observed over a considerable period of time. This is the method which almost every roentgenologist employs during his training period. The trained roentgenologist, however, may follow a less tedious procedure. He may establish the diagnostic criteria which he is seeking by comparing the appearance of a representative number of tuberculous lesions produced on films with which he is familiar (for example, 14×17 inch roentgenograms) with those produced on films with which he is unfamiliar. Such a method was used by the roentgenologist referred to above.

In summarizing, it is evident that all of the newer roentgenological methods which are in use today can be considered acceptable from a diagnostic standpoint for use in mass roentgen surveys for tuberculosis control. It is extremely important, however, that the interpreter of the films clearly understands the diagnostic criteria of the roentgenographic process which is employed. Failure to do this will immediately introduce a large number of diagnostic errors.

R. H. M.



Physical Examination at Induction

Standards with Respect to Tuberculosis and Their Application as Illustrated by a Review of 53,400 X-Ray Films of Men in the Army of the United States[1]

ESMOND R. LONG, Lieut. Colonel, M.C., A.U.S., and WILLIAM H. STEARNS, Capt., M.C., A.U.S.

THIS PAPER IS concerned with that section of the Army standards of physical examination having to do with diseases of the chest, particularly tuberculosis, and their application, as shown by a review of 53,400 chest x-ray films of inducted men.

The standards for chest disease were prepared by the War Department with the advice and assistance of a subcommittee of the Division of Medical Sciences of the National Research Council, in conformity with a general practice of the War Department in the formulation of physical standards. Since the August 1940 edition of Mobilization Regulations, several modifications have been adopted as the need for certain changes has become evident. Inasmuch as definite standards in regard to acceptable and non-acceptable tuberculous lesions inevitably invite criticism, it might be well to examine the steps through which the present standards were evolved.

Originally, in 1940, the primary concern of the committee was that x-ray examination of the chest be made an integral part of the physical examination of every man before acceptance by the Army. The standards, as proposed at that time, while specifying that all active cases of tuberculosis should be excluded, did not define limits as to the size and number of healed lesions which might be considered acceptable. Rather, certain broad principles were set forth and much was left to the judgment of the individual examiners. In theory, this would seem to be the logical and perhaps ideal type of directive. It became evident, however, as the speed of mobilization increased, that it was necessary to adopt quite arbitrary standards rather than expect examining physicians to rely on quick judgment in the thousands of cases showing evidence of apparently healed or inactive lesions. These arbitrary standards, which permit the acceptance of certain inactive states, are based in general upon the size and number of lesions. As will become apparent later in this discussion, the conspicuously arbitrary nature of the limits has been tempered by certain provisions of the present standards. These will be discussed in relation to the infiltration of tuberculosis of re-infection type and then in respect to the calcified lesions of healed primary tuberculosis.

Limits for healed, infiltrative tuberculosis are both qualitative and quantitative. In the first place, to be acceptable such inactive lesions must present a strand-like or dense nodular appearance and, according to the expressed provision of MR 1–9, may not exceed a total area of 5 sq. cm. as projected on a conventional 14 × 17-inch film. Deferment in these cases is required until "subsequent examination demonstrates that the lesion is stationary and not likely to be reactivated." It is stated that the minimum period of time to determine this is six months, that it must be recognized that either progression or regression of the lesion indicates instability, that clinical judgment, taking into consideration other factors, including age and race, must be exercised in estimating the likelihood of reactivation, and finally that experience indicates a greater likelihood of reactivation of a lesion that appears to be stable in persons under twenty-five years of age than in older persons.

In this connection, it should be observed that, in the general preface to the outline of physical standards, it is specifically stated that examining physicians are to consider the standards as a guide to discretion, not to be construed too strictly or

[1] Presented before the Radiological Society of North America at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

arbitrarily. It may be assumed that this provision applies to all sections of the Regulations, including that devoted to the chest. Whatever may be the defects of the regulation on deferment, to which reference was made in the preceding paragraph, practically it has proved useful and it is believed few cases of tuberculosis have developed from lesions of extent and character considered acceptable after the required period of deferment.

With regard to standards for primary lesions, the situation is somewhat more complex, since there are two conflicting schools of thought on the pathogenesis of reinfection type tuberculosis. On the one hand are those who believe the incidental finding of large or extensive calcified residues of primary tuberculosis is of little or no significance for the future, possibly indicating unusually high, or perhaps even enhanced resistance, and on the other, those who feel that large and numerous calcified residues are evidence of a massive infection, not necessarily entirely healed and possibly associated with unrecognized lesions elsewhere in the body. The occasional finding of a caseous center containing living tubercle bacilli on section of large, apparently well calcified nodules and nodes has been cited as evidence of the latent danger of such lesions.

After numerous requests for exact specification of limits for acceptable calcified lesions, standards were set "arbitrarily to provide an objective basis on which the examiner may render a decision." These lesions were defined as follows, all measurements referring to single, standard 14 × 17-inch direct projection roentgenograms:

"*a.* Calcified residues of lesions of the intrathoracic lymph nodes, provided none of these exceeds an arbitrary limit of 1.5 cm in diameter and the total of such lesions does not exceed five.

"*b.* Calcified lesions of the pulmonary parenchyma, provided the total of these does not exceed ten, and one of these may equal but not exceed 1 cm in diameter; but none of the remainder may exceed 0.5 cm in diameter."

It was specified that in the roentgenogram such calcified lesions should appear isolated, sharply circumscribed, homogeneous, and dense.

As a result of such exact mathematical limits, decisions as to acceptance or rejection were reached mechanically in many cases rather than clinically. In succeeding months complaints were received from all parts of the country that men who were perfectly healthy had been kept out of the Army by rigid interpretation of the standards. This was perhaps inevitable in view of the exact limits set forth in the Regulations and in the absence of qualifying statements. Therefore, in a subsequent revision, dated Oct. 15, 1942, a paragraph of explanation was added with respect to the calcified lesions. Quotation of a single sentence from this paragraph will serve to show the liberalizing effect of the revision: "Further consideration may be given to the acceptability of persons with calcified lesions of this type (*i.e.*, in excess of the arbitrary limits) where the state of health in all respects clearly warrants the opinion that the lesions in question are healed." The type of consideration to be given, clinical in character, was then indicated.

In summary, it will be remembered that the first standards left the decision with respect to these calcified lesions to the judgment of the examining physician. Then, when that approach was shown by experience to be impracticable, decision as to acceptance was put on a basis which proved too arbitrary. The present regulations represent a combination of the two approaches, the arbitrary limits being modified by the specific statement that clinical judgment is to be used and a man considered for acceptance if, after careful examination, there is every reason to believe him to be in good health and the lesions well healed. The present modification of the standards is known from personal observation to have proved satisfactory, and many men, rejected on the basis of strict interpretation of the arbitrary limits, have been recalled for reconsideration.

So much, briefly for the standards of

Table I: Summary of Infiltrative Lesions for the Nine Service Commands

Service Command	Number of Films Reviewed	Tuberculous Infiltrates					
		Total		Quest. Signif.		Significant	
		Actual	Per 10,000	Actual	Per 10,000	Actual	Per 10,000
I	4,650	21	45	16	35	5	10
II	5,550	25	45	18	32	7	13
III	7,400	44	59	36	48	8	11
IV	8,400	38	45	27	32	11	13
V	6,050	31	51	23	38	8	13
VI	3,750	8	21	6	16	2	5
VII	4,350	14	32	11	25	3	7
VIII	8,250	53	64	21	25	30	36
IX	5,000	37	74	15	30	22	44

examination. The application of these standards will now be discussed in the light of a review of 53,400 chest x-ray films representative of the men accepted at 89 induction stations in the United States during the summer and fall of 1942.

The films reviewed in this study were random samples from the thousands sent in from each induction station for filing by the Veterans Administration and are believed to provide a fair index of the quality of work at the stations at the time indicated. The great majority of the films received were 4 × 5-inch photoroentgenograms, now almost universally used by the Army induction stations. These with few exceptions were stereoscopic views, which in this type of photoroentgenography are much to be preferred to a single view. A few small stations were still using conventional 14 × 17-inch films as a routine method of screening. Paper films were used by all stations in one service command and by a few stations in another.

In general, 500 to 1,000 films from each station were reviewed. It had been hoped to read at least a thousand films from each, but the time available to devote to the project was insufficient to accomplish this. Instead, the review has been made roughly in proportion to the population of the various service commands.

The primary intent of the standards is to exclude active tuberculosis and, in so far as possible, tuberculosis likely to be reactivated under the stress and strain of military life. Unfortunately, this review would indicate that a certain number of active cases have slipped through the induction stations. The accompanying table indicates, by service commands, the ratio of such cases to the number of men inducted. On the basis of these figures one may make estimates on which plans may be based for the care of tuberculous patients by the Army and the Veterans Administration. The case rate in seven service commands would seem, however, to provide a fairer index than that of all nine service commands, as temporary local difficulties in a minority of the stations in two commands appear to have been responsible for the high rate in those areas.

For the most part, the lesions considered as significant in this review were apical and infraclavicular infiltrates of "soft" appearance, minimal in extent. Many of them seemed quite obvious, but a certain number could easily be missed unless one inspected the 4 × 5-inch views singly as well as stereoscopically. More difficult to explain is the overlooking of several cases of moderately and far advanced disease. It has been discovered that clerical errors were responsible for the induction of some of these men.

The rather consistent ratios for "significant" lesions, 10 per 10,000 for one service command, 11 per 10,000 for another, and 13 per 10,000 for three other commands, and the low rates of 5 and 7 per 10,000 for two service commands (the latter representing, incidentally, the low tuberculosis area of the United States) are believed to provide a basis for a reasonably accurate estimate as to the number of cases of

tuberculosis in the Army. As already indicated, the rates of 36 per 10,000 for one service command and 44 per 10,000 for another are misleading in view of the fact that a small number of stations were responsible for the marked deviation of the whole from the average for the country.

In addition to the apparently significant lesions, 173 infiltrates, considered to represent inactive tuberculous lesions of reinfection type, were discovered, a rate of approximately 35 per 10,000. This group of most of the lesions listed in this group may have been demonstrated before induction. Because of the lack of information, however, as to which of these lesions have been so studied, no valid comparison of the work of the service commands can be based on these figures. Further, it should be pointed out that the number of such lesions diagnosed will, at least in part, be dependent upon the technical quality of the films and the corresponding ease with which small scarred lesions are seen.

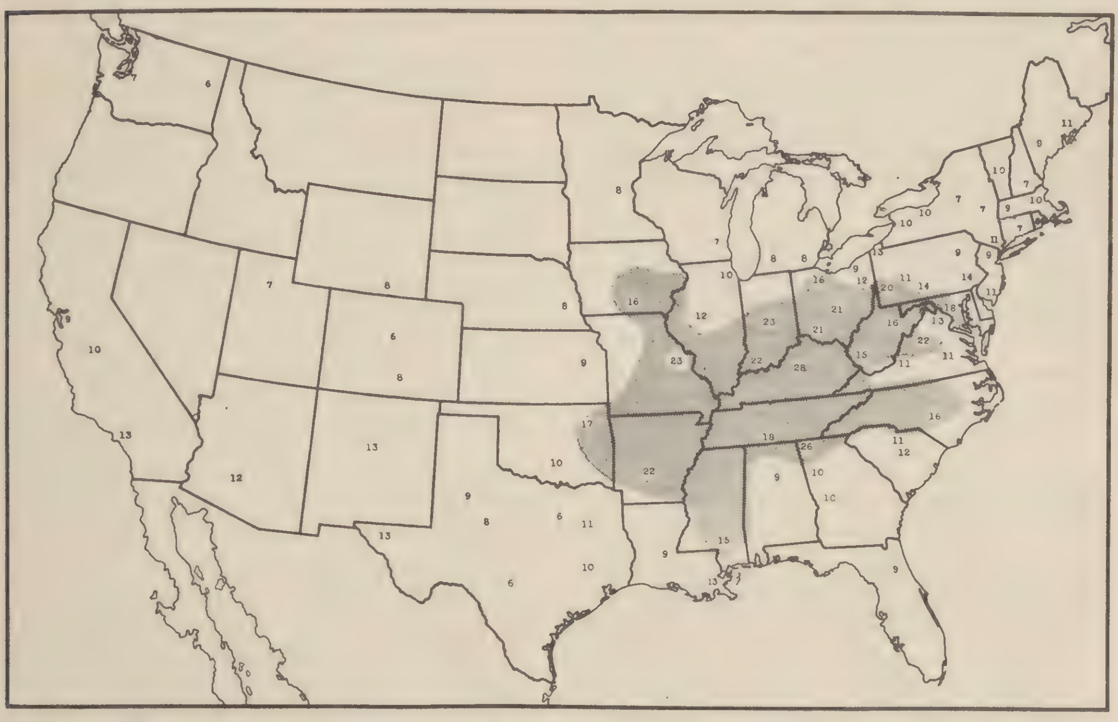


Fig. 1. Incidence of calcified lesions in chest films of inducted men from 89 induction stations. The figures represent percentages for the regions marked. In the shaded area more than 15 per cent of the films of accepted men showed pulmonary calcification.

is composed of infiltrates of a character and extent which the standards specify as acceptable after deferment until subsequent examination demonstrates that the lesion is stationary and not likely to be reactivated.

From personal observation of the work at various induction stations, it is known that men in whom infiltrates of this type are diagnosed usually are accepted only after the required period of observation; so there is reason to hope that stability

The incidence of calcified lesions presumed to represent healed tuberculosis corresponds to the now well known pattern of regional differences in the United States. High incidence (over 15 per cent) was noted in a region bounded roughly by Fort Oglethorpe, Georgia, Jefferson Barracks, Missouri, Little Rock, Arkansas, and Columbus, Ohio. In general, the calcifications noted in the films of men from this region were considerably larger and more extensive than those in men from

Table II: Pulmonary Calcifications
(Percentage in Films Read)

Service Command	Acceptable*	Excessive
I	8.8%	0.06%
II	9.3%	0.14%
III	13.6%	0.20%
IV	13.9%	0.29%
V	18.0%	0.55%
VI	8.4%	0.08%
VII	10.3%	0.11%
VIII	11.3%	0.23%
IX	9.1%	0.14%

* As specified in MR 1-9, March 15, 1942.

other parts of the country. Also, disseminated "miliary" calcifications, variously believed to represent healed residuals of a post-primary hematogenous dissemination of tuberculosis or perhaps, in some cases, a healed fungous infection of the lungs, seemed relatively more frequent in this area.

As the figures with respect to the calcified lesions may be of epidemiological interest to some, a graphic record of the incidence of calcification in accepted men in and around the area under consideration is added (Fig. 1).

The term "excessive" is used to indicate those calcified lesions designated as not acceptable, by reason of their size or number, under the old standards, but acceptable under current regulations, "provided the report of the physical examination and the chest x-ray films have been reviewed and acceptance has been recommended by a medical examiner specially qualified in the diagnosis of diseases of the chest."

At this point it should perhaps be repeated that the apparent emphasis on calcified lesions should not be allowed to obscure the primary intent of the standards, the exclusion of active tuberculosis and tuberculosis likely to be reactivated. Preoccupation with the easily seen calcified residuals of primary tuberculosis must not divert the examiner's attention from the small infiltrative lesions of re-infection type tuberculosis which, especially in the early stages of development, may appear only as vague and ill defined shadows, but which are of infinitely more significance for the future.

It is not considered appropriate at this time to present a detailed report indicating the results of the interpretation for each induction station. It is believed that a summary by service commands will serve the purpose of the present review, indicating those parts of the country where difficulties have arisen making possible the entrance of men with tuberculosis into the Army. It is not the intention of this paper to analyze these difficulties or make suggestions for the further avoidance of error. Needless to say, those officially concerned are informed on the results of the survey and appropriate steps are in course to avoid repetition of the errors uncovered.

SUMMARY

Roentgenologic chest standards for examination of men at induction were drawn up to prevent the acceptance of men with active pulmonary tuberculosis or inactive tuberculosis that might be reactivated by the strain of military service. Since the original formulation of the standards, several changes have been made with regard to inactive lesions. According to current regulations very small infiltrative processes are considered acceptable if their stability has been satisfactorily demonstrated by observation after a period of deferment. Small, well calcified lesions of primary tuberculosis are accepted without question, and large and numerous lesions of this type may be considered for acceptance if the subject examined is twenty-five years old or more, if the nodules are dense and discrete, and finally if thorough clinical examination yields no indication of active disease.

A study was made of the effectiveness of the examination, as revealed in films of accepted men filed with the Veterans Administration in the summer of 1942. A review of 53,400 films from 89 induction stations indicated that a certain number of cases of infiltrative tuberculosis, clearly inacceptable according to the regulations, have escaped detection at the induction stations. The number of such instances is small in two service commands, inter-

mediate in five, and large in two. Steps to remedy defects in the examination are in course.

The incidence of healed primary tuberculosis in accepted men, as indicated by the presence of calcified masses in the lungs and hilum lymph nodes, was found to vary geographically in a manner quite in accordance with current general observation, a high rate prevailing in a region in the east central portion of the country.

War Department, Office of the Surgeon General
Washington, D. C.

DISCUSSION

Lieutenant Colonel de Lorimier: Because of the amount of controversy relative to stipulations pertaining to chest examinations as described in Army Regulations, I believe that I should re-emphasize the point that these regulations are intended merely to serve as a guide. In case too literal an interpretation of them is made, review boards function to clear discrepancies. Credit is due particularly to Colonel Long for enforcing the most practical decisions and working upon improvements of a technical nature to provide for the highest quality of graphic records, thereby insuring the most trustworthy roentgenographic records that will later serve as legal records.

The data cited by Colonel Long indicate percentages of oversight by our Army examiners. Many of the mistakes represent liabilities for our Government. These are costly mistakes. Statistics of the last great mobilization indicate that on the average each such mistake, which leads to compensation, costs our taxpayers $10,000 to $15,000. Moreover, in many instances, there was dissemination of disease by the individuals involved resulting in a multiplication of the compensation requirements. Furthermore, most of these mistakes account for man-days lost to the Service.

Surely these studies indicate the great responsibility which rests upon doctors who are entrusted with this work. In particular, I would refer to the roentgenologist. Statistics such as those reported by Fellows and Ordway would seem to be substantial proof that few cases of minimal parenchymal lesions are likely to be identified by the use of the stethoscope—this fact in direct contrast to the trust which can be placed in roentgenography. But the data presented indicate a very considerable error even with roentgen studies. Serious deliberation about this problem prompts the suggestion that blame might be attributed to a variety of factors:

First, lack of appreciation by the individual examiner as to the real responsibility which has been entrusted to him.

Second, delay in putting into practice the long ago accepted official plan of procedure.

Third, overtaxation of the visual and mental acumen of the average pair of eyes and the human brain.

With respect to the first of these, it must be admitted that a professional diet of viewing chest films all day long and day after day is not ordinarily stimulating. To offset the doldrum character of this routine, we have attempted to encourage each officer to assemble data such as Colonel Long, independently, has accumulated. There is a wealth of knowledge to be gained from this tremendous survey. It should be possible for each examiner to obtain statistical information relative to no less than 50,000 or possibly as many as 250,000 Americans and in the end to learn of the incidence of one or another condition for various sections of our country.

Referring to the matter of delay in putting into practice the official procedure, I would remind you that there were difficulties in setting up the equipment and in distributing materials so suddenly to every section of the country. The official procedure calls for the use of 4 × 10-inch single emulsion films, providing for photographing the fluoroscopic image and viewing two images stereoscopically. The standard 14 × 17-inch films may be used to clarify doubtful evidence. Some of the examiners are known not to have viewed their films stereoscopically. Moreover, in many instances, the contrast characteristics of the photoroentgenograms have been so great as to obliterate too much.

As previously stated, for this procedure, it is the conviction of our group at the Army Medical School that higher than conventional kilovoltages should be used and that the single emulsion rather than duplitized films are needed. The importance of these factors is now being widely recognized.

At present, we do not know the limit as to the number of cases which the average person can alertly analyze in a day—and day after day. Since we doctors belong to no union, we tend to a determination of finishing any task which is set before us. In some instances we hear of a single examiner studying even more than 600 cases in a day. Personally, I do not believe that I can be trusted to analyze thoroughly more than 400 cases each day for a period of days.

Edwin C. Ernst, M.D. (St. Louis, Mo.): I have been very much interested in this most timely review of such a large group of draftee examinations, especially the roentgen evaluation of the diagnostic chest criteria set up by the Army for the interpretation of early tuberculous lung infections.

It would seem to me that the diagnostic significance of multiple sharply defined calcifications within the lung fields—excluding upper interspace apical involvements as very suspicious roentgen evidence of early tuberculosis—has been over-emphasized and that this over-emphasis has not been in keeping with the experience of many of us who are privileged to

review thousands of chest films every month. The diagnostic problem of sharply defined lung calcifications and excessive thickening of the hilar and peribronchial tree was discussed pro and con prior to our entrance into the last war. At that time the literature available upon this subject was very meager; nevertheless, those of us who saw early service in France soon realized their relative unimportance as pathognomonic roentgenologic signs of active incipient tuberculosis.

In 1917–18, at Rouen, France, Base Hospital Unit No. 21, facilities were made available for Dr. Eugene Opie and myself to examine, pathologically and roentgenologically, hundreds of lung specimens of British and American soldiers. After calcified lung fields had been "spotted" on large x-ray plates, the autopsy specimens were then minutely re-examined roentgenologically and histologically. Approximately 70 per cent of our American soldiers presented varying degrees of excessive lung calcifications as compared to but 30 per cent of the British. The reverse was true in reference to the mesenteric calcifications of autopsy specimens. Approximately 20 to 30 per cent of the American soldiers showed calcifications of the mesenteric node structures as compared to 70 per cent in the British group examined.

Time will not permit me to discuss all of the clinical interpretations of these research observations in relation to the resistance factors of acquired early or late tuberculous infections. Age, of course, plays an important role as a predisposing factor in pulmonary tuberculosis. Many other clinical factors must be given due consideration. Semi-calcified indistinct fibrotic densities in the peripheral apical areas of the lung are likewise suspicious findings without controlled serial x-ray studies. Recently, however, I reviewed a large group of chest films of cement workers, made annually, in whom multiple hilar and peripheral calcifications were present, and yet not a single worker had contracted tuberculosis over a period of five to nine years, although the usual percentage of expectant tuberculous infections were noted in the non-calcified areas of relatively clear lungs.

I am happy to hear Colonel Long make the statement that the published Army calcification rules, or their roentgenological diagnostic criteria of minimal tuberculosis, are in the process of modification by official decree. Some of us have been very much embarrassed in our medical practices by the apparent arbitrary standards of diagnosis by the Army, limiting hilar calcifications to four in number, while six nodes of a given size are sufficient reason for rejection. Let us not be unmindful of the mental anguish and economic stigma which will most certainly follow many of these rejected applicants throughout their lifetime.

In a group of 24 men observed during the past month, and previously examined by me three to five years prior to their present examination, all of whom were rejected by Army Boards as tuberculosis suspects, not a single one presented suspicious history findings, and even now they show no evidence of clinical tuberculosis. These cases and hundreds of others examined each month and rejected by the Army are my reasons for questioning some of the conclusions presented in this paper.

In the light of practical experience of at least some of us in the diagnostic field of early pulmonary tuberculosis, doesn't it seem logical that the Army regulations, heretofore discussed, should be reviewed in their entirety by a competent group of internists, pathologists, and radiologists, rather than modified by means of a special communication?

Otherwise—lest we forget—what will happen to a post-war veteran if he discovers at the time of his discharge from the Army that he had six calcified nodes instead of four and, therefore, is in a position to demand compensation for life as a tuberculosis suspect?

W. Edward Chamberlain, M.D. (Philadelphia, Pa.): Four-by-ten stereoscopic roentgenograms, as made at induction stations, are remarkably satisfactory from a technical standpoint. Experience shows, however, that even when these photoroentgenograms are entirely above reproach from a technical standpoint, it is possible for the roentgenologist to overlook an important lesion. I speak from experience.

A few months ago, at the Philadelphia Induction Station, a younger colleague placed a "4 × 10" in front of me with the question: "Is that calcification at the left hilum above acceptable limits of size?" I focused my attention on the hilar calcification and expressed the opinion that it was within acceptable limits. A little later we learned that two months earlier, when this recruit had applied for a commission, he was rejected because of a reinfection type tuberculosis. On reviewing the film, we discovered a significant lesion in the right upper lobe.

A few weeks later I again missed a perfectly definite reinfection type tuberculosis in a "4 × 10" of excellent quality. The day was saved in this instance by Capt. James G. Whildin, when he reviewed the film for identification purposes. Captain Whildin then called my attention to the fact that such errors of omission can be prevented by making it a practice to view the "4 by 10's" directly, without lenses or apparatus, before or after viewing them stereoscopically. The use of the stereoscope would seem to give one "tubular vision" with increased likelihood of limiting the study to some part which attracts attention rather strongly at first glance. By looking at the film outside of the stereoscope, on an ordinary illuminator surface, one is apparently much less likely to overlook an important lesion.

I do not mean to belittle the value of the stereoscope. The point I am making is that each film should be looked at both with and without the stereoscope, if errors are to be avoided.

ARMY X-RAY EXAMINATIONS OF THE CHEST

DURING the past eighteen months, a number of directives have been circularized pertaining to requirements of x-ray examinations of the chest prior to acceptance or prior to discharge of one or another group of individuals concerned with military service (AR 40-105, C 5, August 17, 1940; AR 40-100, September 10, 1940; AG 201.6 ORC, 9-6-40, R-A, December 28, 1940; AG 702, January 9, 1941; War Department Circular No. 146, July 22, 1941; and MR 1-9, January 16, 1942). This procedure now pertains to all military personnel, candidates for commission, enlistment, re-enlistments, and inductees. Similar examinations are conducted prior to the departure of military personnel for duty outside of the United States (War Deparment Circular No. 270, December 27, 1941).

The importance of these examinations does not seem to be fully understood. They are intended to serve a three-fold purpose: (1) to lend to completeness in the examinations and thereby serve the individual, (2) to segregate cases having diseases of the chest—particularly, active or potential cases of tuberculosis—thereby serving in an epidemiological manner to protect the group, and (3) to provide irrefutable graphic records which might be used at any time during the life of the individual, in case of pension claims. Thus, it is intended that these film studies serve both for aid in immediate analyses and for comparative evidence in later years—this latter purpose being synonomous to a legal record.

These aspects of the x-ray examinations indicate the serious trust which is officially placed upon them, and the serious responsibility on the part of those directly engaged in or supervising either the technical or the interpretation activities.

The problems concerned with interpretation are multitudinous. They should be handled as detailed diagnostic problems by doctors acquainted with the fields of diagnostic roentgenology or phthisiology and with the guidance of the specific regulations.

The trust of the roentgenographic method of studying the chest might be summarized by the conclusions of Drs. Fellows and Ordway, of the Metropolitan Life Insurance Co. They have stated that "if one can assume that the x-ray examination reveals 100 percent of the lesions of pulmonary tuberculosis our results are:

revealed by x-ray, 100 percent; revealed by fluoroscopy, 87 percent; revealed by physical examination, 36 percent; revealed by symptoms, 33 percent."

This evaluation was based upon routine use of 14 x 17 inch film studies whereas the Army has adopted stereoscopic 4 x 5 inch studies (i.e., for stereoscopic pairs, 4x10 inch films) wherever possible, and it is believed by many who have conducted these studies that they are even more trustworthy than the single 14 x 17 inch f lms.

The decision that x-ray examinations of the chest be adopted was not based upon enthusiastic expressions by roentgenologists alone. The expression of the Subcommittee on Tuberculosis[2] of the Division of Medical Sciences, National Research Council, carried considerable weight. On July 23, 1940, this group summarized their opinions as follows:

"(1) At least 75 percent of early active tuberculosis can be discovered only by x-ray examination.

"(2) About 1.0 percent of the male population of military age has active tuberculosis, most of which can be detected only by x-ray examination.

"(3) A high proportion of cases of early tuberculosis, detectable only by x-ray examination, is likely to break down under such strain as that entailed by military duty, incapacitating them for further service and making them a menace through contagion to their comrades.

"(4) X-ray examination is more expeditious than physical examination, thereby saving considerable time in the general examination.

"(5) X-ray film examination furnishes a permanent and authoritative record which may be useful in subsequent medicolegal adjustment.

"(6) Other conditions than tuberculosis which would make the registrant unfit for military duty may be discovered by x-ray examination.

"This procedure will amply repay the cost by saving of effective military manpower, and reducing the ultimate cost to the Federal government in pensions."

These x-ray studies might be accomplished by a variety of methods. A comparison was made with consideration of the standard 14 x 17 inch stereoscopic films, the use of single 14 x 17 inch films, the use of two 14 x 17 inch paper films or single paper film, the use of a single 4 x 5 inch film or stereoscopic pairs of the

same dimensions, the use of single 35 mm. films or stereoscopic pairs of that dimension, and fluoroscopy. It was finally decided that the stereoscopic 4 x 5 inch studies were most appropriate for our purposes. This decision was based on a number of features.

Foremost of these was the consideration of "trust for mass studies." At the examining stations in the Army, roentgenographic procedures must be accomplished on a very large scale. Hundreds of subjects must be examined in a day. The positioning of the men, the handling of the films, and their processing—and then the study of the films—must be accomplished rapidly, almost like clockwork. The 4 x 5 inch films were found to be relatively easier to handle under these conditions and they were the easiest to study, particularly if prepared stereoscopically.

Costs were considered, and in this respect, too, the 4 x 5 inch film studies were favored, for with them a stereoscopic pair was estimated to be much less than a single 14 x 17 inch film either of the conventional or the paper type.

The legal aspects dismissed the possibilities of utilizing fluoroscopy and compelled plannings as to storage. The storage problem was no insignificant one. If 14 x 17 inch standard films were to be used and two such allowed for each examination (i.e., simply allowing for a single film study prior to admission, and again prior to discharge), for 4,000,000 such examinations there would be required cabinet accommodations equivalent to no less than 20,000 standard cabinet drawers to accommodate a row of such films which, if placed back to back, would extend for approximately eight miles! No less than 500 tons of film would thereby be concerned, an item of considerable importance in times of wartime preparations. Similar weight and slightly greater bulk would have pertained to 14 x 17 inch paper films. These values are reduced to approximately one-sixth when using the 4 x 10 inch film (as provided for making the stereoscopic pair of 4 x 5 inch images). Though the use of the standard film is still authorized, particularly where further studies are desired, it is believed that these aspects should be considered and, wherever possible, the small films should be used.

The unusual trusts which pertain to these studies prompt special considerations and considerable emphasis with respect to provisions of a technical sort which might serve for producing the maximum of roentgenographic quality and durability of the films. In particular, thought should be given to proper focusing of the lens, the use of a single emulsion film, the application of a

high kilovoltage technique, the use of the wafer grid, and the importance of adequate washing of the films.

The technical procedure concerned is a photographic one. The camera (containing the lens) is mounted on to the fluoroscopic screen. There are a number of components to the lens. In case these components be not properly adjusted, one with another, and if the entire lens be not properly focused to the plane at which the film is positioned, it will be impossible to obtain sharpness of detail in the 4 x 5 inch photograph of the fluoroscopic image. Careful focusing of the lens is one of the most important provisions concerned with this procedure. As far as contracts which have been made in the past are concerned, the Army has included payment for complete checking of the installation, including the proper focusing of the lens. Therefore, in case difficulties of this sort are noted, representatives of the manufacturer of the fluoroscopic camera unit should be consulted and arrangements should be made for making whatever adjustments are necessary. Thereafter, care should be taken that the adjustment be not tampered with, for, unless the film shifter be changed or warped, it should not be necessary to make any readjustments. Because of the large dimensions of the lens required for this unit there are likely to be aberration irregularities concerned with its function. Ideal focusing should be accomplished for the mid-lung zones—sacrificing perfection of focus for the central and peripheral portions of the film, if necessary.

The energy responsible for the sensitization of the emulsion, in this procedure, is light—rather than x-ray energy. Light rays are easily reflected and refracted. For this reason it is important that the single emulsion films, having nonhalation backing, be used. When using the conventional x-ray film, which is duplitized, approximately 15 to 30 percent of the photographic density is produced upon the second, that is, the back layer of the emulsion. There is so much dispersion of the rays in their traversing the front emulsion and the film base that this second image is blurred. When it is superimposed upon the image of the front emulsion the composite image is lacking in detail. With the single emulsion film, loss of detail due to reflection or refraction of the light rays is not so likely. Particularly in the case of small dimensions, such as 4 x 5 inches, it is very important that the maximum of sharpness in detail be obtained. Single emulsion films are being supplied, but occasionally it is necessary to cut a conventional film in order to meet an emergency. In such cases, the shortcomings should be realized. Certainly every effort should be made to

maintain a sufficient supply of the single emulsion films.

Because of the fact that the fluoroscopic image has high contrast and since photography of that image ordinarily increases the amount of contrast, it is important to obviate the end result of excessive contrast. In conventional chest roentgenography, the kilovoltage values are usually within the 65 to 75 Kv.P. range. When such kilovoltages are used for the small film chest studies, not infrequently the contrast characteristics are so great that the mid-lung zones are overexposed while the peripheral portions of the chest are markedly underexposed. There is a peripheral "halo" whereby adequate visualization may be lacking in very important regions—the apices and outer thirds of the lungs, for instance. To obviate this situation it is advisable to use relatively higher kilovoltages than ordinarily used for chest studies and to insert a wafer grid between the chest and the fluoroscopic screen when secondary radiation might be bothersome. When using the wafer grid, it is necessary to double the exposure over that which would be required without the use of the grid. Therefore, for the sake of avoiding unnecessary punishment of the x-ray tube, it is advisable not to use the grid for chests of relatively small thickness. Usually, a thickness of 24 or 25 centimeters, or greater, can be considered as calling for the use of the grid. The following outline of technical values has been found practical:

TABLE 1

Photoroentgen Technique

(Based upon a balanced transformer function, good line conditions, and a focal-fluoroscopic screen distance of 36 inches)

Cm. Thickness	Kv.P.	Without grid		With grid	
		Ma.	Time	Ma.	Time
16	72	200	1/10		
17	74	200	1/10		
18	76	200	1/10		
19	78	200	1/10		
20	80	200	1/10		
21	82	200	1/10		
22	84	200	1/10		
23	86	200	1/10		
24 *	88	200	1/10	200	1/5
25 *	90	200	1/10	200	1/5
26 *	90	200	1/10	200	1/4
27 *	90	200	3/20	200	3/10
28 *	90	200	3/20	200	3/10
29 *	90	200	1/5	200	2/5
30 *	90	200	1/5	200	2/5

* Recommend use of grid on these exposures.

When exposures greater than 40 milliampere-seconds are required, it is advisable to allow from 3 to 5 minutes' rest for dissipation of heat by the x-ray tube, following the making of a stereoscopic pair. This precaution will lend to greater tube life.

Particularly, considering the legal aspect of this project, there is hardly a precaution deserving of greater emphasis than that with respect to adequately washing the films. Inadequate washing of them will result in their early deterioration. Unless the salts of the fixing bath be removed, the sulphur radical will combine with the silver in the film emulsion to produce a brownish discoloration; later, the film will become brittle and possibly it will fragment. These changes may occur within a few months or within a few years. We are actually facing a new problem. Pension claims may occur at any time. Even ten, twenty, or thirty years following the exposure there may be reason to compare findings with those at the time of admission into the service. Certainly, stained or fragmented films will not then be trusted. Careless washing may result in unwarranted grants of pension, and the ultimate expenditure of as much as from $15,000 to $20,000 per individual concerned.

Ordinarily, films should be washed in running water for as long as one hour. This time requirement might be reduced where a cascade type of washing is provided. At induction stations, the activities are usually so rushed that time for adequate washing cannot be allowed during the actual processing of the candidates. In such a case, the policy should be to include only a casual washing (of perhaps ten to fifteen minutes) ; then to accomplish the study of the films and thereafter to provide for a second washing. The latter might be accomplished by having water flowing over them throughout the night, and drying them for filing the following morning prior to beginning the regular run of that day's activities.

Adequacy of washing should be checked with the use of an indicator. Ordinary potassium permanganate serves well for this purpose. A very small crystal of it should be dissolved in an ounce or two of water (distilled water, in case the community water contains an appreciable amount of organic matter) to a concentration such as to provide a light pink color. The quantity should be divided into two portions, one to serve as the control. The wash test is accomplished by simply allowing a few drops of water to drain from a sample film into one of the permanganate solutions. If these drops produce a discoloration from the pink to a colorless or yellow, the evidence is that an excessive residuum

of sulphur has been left on the film and that further washing of it must be accomplished.

It is important to file the films in a cool dry place. The temperature should not be greater than eighty degrees Fahrenheit. The films should be placed in envelopes without their being in apposition to glue or paste surfaces.

Reference should be made to section IV of War Department Circular No. 233, issued November 6, 1941, which describes the requirements as to proper identification of the films and as to ultimate storage of them.

BIBLIOGRAPHY

1. Fellows, H. H., and W. H. Ordway, *Fluoroscopy versus physical findings in detection of pulmonary tuberculosis*, Nat. Tuburc. A. Tr., 33:51-53, 1937.
2. Minutes of the Meeting of the Subcommittee on Tuberculosis, Committee on Medicine, Division of Medical Sciences, National Research Council, held at the National Academy of Science, Washington, D. C., July 23, 1940.

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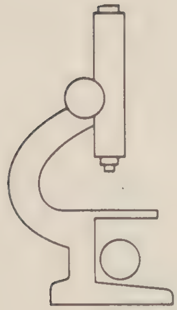

SECTION ROENTGENOGRAPHY IN PULMONARY TUBERCULOSIS*

HUGH M. WILSON

Progress in the art of diagnosis of pulmonary tuberculosis has paralleled refinements in roentgen diagnosis of pulmonary disease. The advances made in recent years have resulted in widespread extensions of roentgenological service in tuberculosis case-finding, not only in clinics, schools, hospitals, and induction centers for the armed forces, but also in industry. This increased demand for routine chest roentgenograms has and will continue to demonstrate many pulmonary lesions in an earlier stage of their life history. Many of the characteristic roentgen signs that simplify recognition and denote or suggest the etiologic diagnosis are lacking in the early lesions.

The particular problem in thoracic roentgenology has always been the obscuring densities of the bony thorax and the thoracic viscera which prevent clear visualization of small pathological lesions. Stereoscopy is often valuable, but is subject to individual personal skill and the experience of the observer. It is not foolproof and has never been universally accepted. Sectional roentgenography, or roentgenography of the layers of the body, has proved a valuable technical method for resolving confusing superimposed shadows of structures, particularly in the chest where necessary contrast densities are found. There are several technical methods of making sectional studies which have been proved satisfactory in theory and practice.

To avoid serious errors in differential diagnosis it has become necessary and desirable to utilize any or all roentgen technics as well as clinical and laboratory procedures. The roentgen technics include fluoroscopy, conventional roentgenography in various positions, section roentgenography, bronchography, and pulmonary angiography. (Kymography has proved of little value in pulmonary lesions.) Proceeding from the simpler to more complex procedures, diagnostic

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pneumothorax, bronchoscopy, and thoracoscopy are called upon as indicated in the work-up of the problem case. Fluoroscopy and a single postero-anterior film of the chest may adequately establish a "roentgen diagnosis" of pulmonary tuberculosis in the absence of symptoms or positive sputum. The acceptance of roentgen findings as etiological proof may be necessary *pro tempore*, but it is always hazardous and should be deplored.

Contribution to the clinical evaluation of many pulmonary lesions is possible through sectional examinations and may at least aid in directing the next step in the diagnostic work-up. During the last four years some fifteen hundred section examinations have been carried out in the Department of Radiology of the New Haven Hospital. Approximately one-half of this number were section studies of the thorax. Two hundred and eight examinations were for known or suspected cases of pulmonary tuberculosis. Although this material does not lend itself to statistical analysis as to the relative value in diagnosis, sufficient experience has been gained to justify the impression that the method is meritorious in improving our appreciation of the pathological changes in both early and advanced tuberculosis. It must be used, like all roentgen technics, as a tool for clearer visualization of anatomical structures and pathological processes. It cannot establish more than a presumptive or working diagnosis to be proved or disproved by other methods.

One of the striking contributions of section studies is the visualization of the air pathways of the larynx, trachea, and bronchi in cases suspected of harboring endobronchial infection with the sequelae of stenosis and bronchiectasis. The following case is illustrative. (See Fig. 1)

Case I (B22486), a female, aged 24, was admitted to the New Haven Hospital on Dec. 7, 1941. The patient had been in good health, except for attacks of acute sinusitis, until one year before admission. At that time she "caught a cold" following which she began to have "asthmatic attacks." Four months before admission she developed what was interpreted as a pneumothorax on the left side, and was confined to bed for 15 days. The pneumothorax was said to have absorbed after an unsuccessful attempt to aspirate the air. Three weeks before admission she suffered a second similar episode, associated with pain and shortness of breath, which confined her to bed. There was gradual subsidence of the pain but persistence of the wheezing respirations. The patient had lost six pounds in weight since the onset of her illness. There was no history of hemoptysis, night sweats, anorexia, or after-

noon fever. On physical examination there was some dullness to percussion over the entire left lung. Many inspiratory and expiratory moist râles were heard over both sides, somewhat more marked on the left, with diminished spoken voice sounds. Conventional stereoscopic films of the chest revealed minimal dense mottling at the left apex in the infra-clavicular region. Fluoroscopy and roentgenography in inspiration and expiration revealed a slight shift of the heart and mediastinum to the right on full expiration. Laminagraphic sections showed a fusiform narrowing of the left main bronchus to one-half its normal diameter. The orifice of the left lower lobe bronchus was twice the caliber of the stenosed main bronchus. On bronchoscopic examination an inflammatory reaction was seen in the mucosa of the left main bronchus. Four centimeters below the carina, just proximal to the opening of the left upper lobe branch, the main bronchus was very narrowed and would not permit passage of the bronchoscope beyond this point. A suction tube was placed through the small opening and bronchial secretions were aspirated. An acid-fast stain of this secretion showed many tubercle bacilli.

Discussion: It seems likely that the two attacks of pain and dyspnea which were interpreted as spontaneous pneumothoraces were probably episodes of expiratory valvular obstruction with obstructive pulmonary emphysema of the left lung. Although tuberculous bronchostenosis of a large bronchus with minimal parenchymal disease is unusual, the effects of extrinsic pressure of enlarged hilar and mediastinal glands upon the air passages is probably too little appreciated. In no sense can section studies be considered as a substitute for bronchoscopy but they may serve as a method of selection of cases deserving bronchoscopic examination.

A common indication for section roentgenography in advanced pulmonary tuberculosis is the demonstration or corroboration of the suspected presence of a cavity. The method is ideally suited for the task of resolving the heterogeneous changes that occur in the extensively diseased lung, and cavities are frequently unequivocally demonstrated by eliminating the obscuring superimposed structures. The healing process of fibrosis, with some retraction, occurs simultaneously with emphysema of the adjacent normal lung in the immediate vicinity. The formation of bullae and pneumatoceles offers difficulties in differential diagnosis and may be confused with tuberculous cavitation. Bullae tend to have thin walls, may lie within the parenchyma or even invaginate an interlobar fissure, and occasionally contain fluid levels. At autopsy the actual presence of a cavity within the lung may be confirmed but the roentgen impression

of its tuberculous character may be disproved in favor of a large pneumatocele or bulla. Section studies of many chronic fibroid apical lesions (clinically healed) have demonstrated large antra hidden behind thickened apical pleura and entirely unsuspected from clinical, laboratory, and conventional roentgen examinations. A large clinicopathologic experience will be required to determine which are epithelialized tuberculous cavities and which are emphysematous bullae, since both can be demonstrated throughout the entire depth of the lung.

Case II (A72375), white male, aged 50, has been under observation at various tuberculosis sanatoria and follow-up clinics since 1935 because of chronic pulmonary phthisis. The patient complains of dyspnea on exertion and has a slight cough productive of very little sputum. Conventional films of the chest reveal extensive bilateral apical pulmonary fibrosis with almost complete opacity of the upper portions of both upper lobes and marked retraction of the pulmonary vessels laterally and superiorly. Repeated concentrated sputum examinations have shown no acid-fast bacilli over a six-year period of observation. Yearly x-ray examinations of the chest have shown no change in the appearance of the fibrotic disease of both upper lobes. Body section roentgenographic examinations reveal, throughout all sections, large, rounded, thin-walled cavities, which in every respect have the appearance of tuberculous cavities. The characteristic displacement of the trachea and the distortion of the bronchial tree are seen in the section films.

Discussion: In the clinical course, over a long period of observation, there is little to suggest that the patient has significant or active disease. The patient looks well, feels well, and has never received more than a minimal rest-cure, following which he resumed and has continued at his work. Examination by section roentgenography serves to raise many interesting questions regarding the nature of the demonstrable cavities and of their clinical significance, particularly by that school of phthisiologists who feel that tuberculous cavities seldom epithelialize completely and are subject to exacerbations of reactivity with positive sputa. It is obvious from the clinical data and follow-up of this patient that the roentgen findings must not be permitted to carry much weight in prognosis or treatment.

Section roentgenography may contribute valuable information in those patients with fulminating ulcerative processes with secondary infection and clinical findings suggestive of pulmonary abscess or bronchiogenic carcinoma.

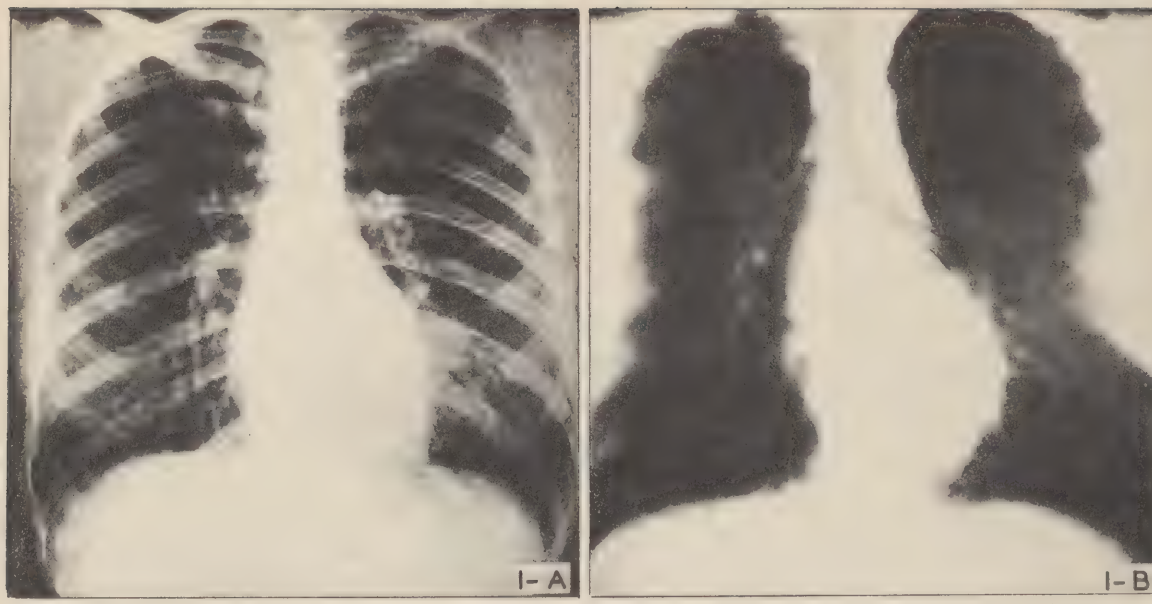


FIGURE 1. (*Case 1.*)

A. Conventional film of chest showing minimal left apical mottling.

B. 8 cm. section roentgenogram showing stenosis of left main bronchus (retouched).

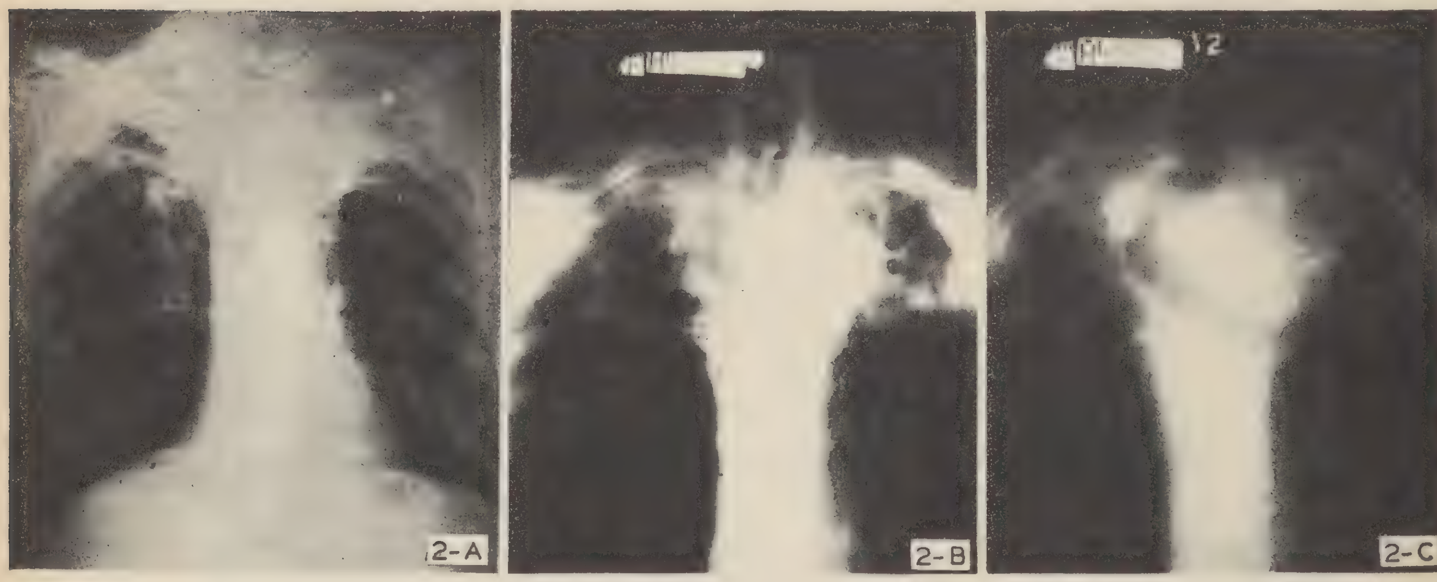


FIGURE 2. (*Case 2.*)

A. Conventional film of chest.

B. 8 cm. section showing extensive cavitation of both upper lobes.

C. 12 cm. section showing tracheal dislocation and cavities in the anterior portions of both upper lobes.

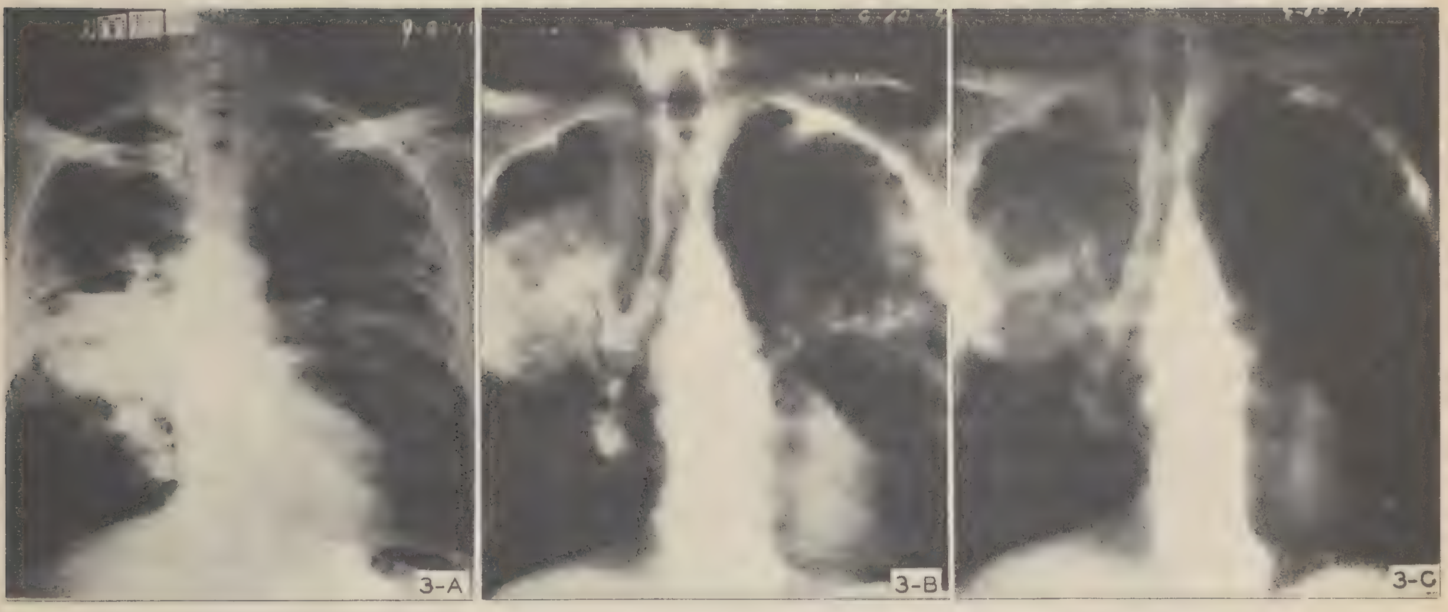


FIGURE 3. (*Case 3.*)

A. Conventional film of chest showing multiple abscess cavities with fluid levels in right upper lobe and minimal pneumonitis in left upper lobe.

B. 10 cm. section showing distortion with multiple points of stenosis of trachea and right main bronchus.

C. 12 cm. section showing thick-walled cavity in right upper lobe.
Note: Marked thickening of paratracheal soft tissue shadow and stenosis at thoracic introitus.

FIGURE 4. (*Case 4.*)

A. Conventional film showing suggestion of infiltration of left upper lobe in paravertebral lung zone.

B. Midline section film showing Y-shaped dilated pulmonary artery arising from left hilum.

C. Pulmonary angiogram showing opacification of pulmonary arterial trunks.

Case III (2423), white male, aged 59, was admitted to the New Haven Hospital with a two-year history of loss of weight, polydypsea, and polyuria. Three weeks before admission he developed a respiratory infection with a productive cough. Physical examination revealed dullness at the right apex, scattered moist râles in this area, and rhonchi throughout the remaining portions of the chest. The temperature was 100° F and the white blood count was 11,600. Fluoroscopic examination of the chest revealed a large area of consolidation in the right mid-lung field with a cavity and fluid level. The lung was emphysematous. The finger-nails were slightly cyanotic with a suggestion of clubbing of the fingers. The urine showed a marked reaction for sugar. Initial sputum examinations failed to show acid-fast bacilli. During the hospital course the patient had temperature rises to 101° F. with marked increase in sputum to 100 cc. daily. Conventional x-ray examination of the chest revealed the previously described abscesses in the right lung field with multiple fluid levels, and pneumonitis involving the right upper, middle, and lower lobes, as well as pneumonitis of the left upper lobe. The possibility of primary bronchiogenic tumor with secondary lung abscess was entertained. On Sept. 16, 1941, bronchoscopy was carried out by Dr. Canfield with the following findings: Four to six centimeters below the carina in the right main bronchus a mass of granulation tissue occluded the lumen. The tissue bled easily. Biopsy was attempted but the tissue was so friable that little was obtained with a forceps. Neoplasm could not be ruled out, but it was thought that the endobronchial lesion was the result of mediastinal lymphadenitis. Body section examination of the chest revealed a marked irregularity of the lumen of the trachea and the right main and intermediate bronchi suggestive of an ulcerative and hyperplastic lesion. There was also narrowing of the lumen of the right upper lobe bronchus and irregularity of middle and lower lobe divisions. The previously noted consolidation and cavitation of the right lung were again demonstrated. In the left lung at the 12-centimeter level a small oval cavity measuring two centimeters in diameter was seen in the left upper lobe. The roentgenographic impression was tuberculous tracheobronchitis with stenosis of the right upper lobe bronchus and bilateral pulmonary tuberculosis with cavitation. A second bronchoscopy in the light of the laminagraphic findings revealed marked irregularity of the tracheal wall. The tracheal rings could be seen, although the mucosa was swollen. An attempted biopsy only scratched the mucosa, a fragment of which was removed. The mucosa of the main bronchus was again seen to be inflamed and swollen without ulceration. The bronchoscopist's impression was that the lesion was submucosal and probably subcartilaginous. Surgical pathological specimens obtained by biopsy of the left main bronchus revealed a gradual transition of the respiratory type of epithelium to pseudostratified squamous epithelium with intact basement membrane. Within the submucosa were numerous chronic inflammatory cells. Pathological diagnosis: Chronic bronchitis with squamous metaplasia of the epithelium. Subsequent sputa

examinations and guinea-pig inoculations were positive for tubercle bacilli. The patient was transferred to a tuberculosis sanatorium on Sept. 30, 1941, where he showed progressive increase in the extent of the disease. In March, 1942, he developed a heavily blood-streaked sputum with repeated hemoptyses. On April 5, 1942, following a series of massive hemorrhages, he expired. Autopsy was not obtained.

Discussion: The cavity demonstrated in the left upper lobe by section roentgenography was entirely unsuspected by the conventional examination. The bilateral cavitation with the extensive changes in the entire tracheobronchial tree contributed strong evidence in favor of a working diagnosis of tuberculosis, although simple lung abscess or abscess secondary to bronchiogenic cancer was suspected from the clinical, bronchoscopic, and conventional roentgen examinations. In both the inflammatory and neoplastic lesions the delineation of the trachea and bronchi by section roentgenograms is valuable to the bronchoscopist in suggesting leads for his endoscopic exploration.

Although the air passages, including trachea and bronchi, and the lung parenchyma offer the primary interest in tuberculous disease of the lung, it has been said that a knowledge of the pulmonary vascular structures is of equal or greater importance in roentgen diagnosis. Until relatively recent years recognition of the pulmonary arterial branches and pulmonary veins has been granted scant appreciation except for the all too frequent and unflattering mistake of their identity as bronchial markings. The following case will serve to illustrate the necessity for roentgen recognition of the normal and pathological vascular shadows.

Case IV (B20727), Italian male, aged 24, was referred for follow-up examination of the chest because a roentgenogram of the chest before induction into the armed forces had revealed pulmonary infiltration of the left upper lung field. The patient had been told he had pulmonary tuberculosis of the left upper lobe and was advised to seek medical care. At the time of his follow-up examination the patient stated that he had a cough for two or three days accompanying a chest cold and he had felt feverish on a few occasions during the past three and a half weeks. The patient volunteered the information that his feverishness might be just imagination, since he was told that he had pulmonary tuberculosis. On physical examination the chest was negative. Respirations, 24; blood pressure, 118/70; tuberculin, negative to 1 mg. O.T. The clinical impression was a question of early tuberculosis. The patient was referred for a repeat x-ray examination of the chest. Stereoscopic roentgenograms revealed thickening of the pleura at the left

apex. A Y-shaped dense structure was seen in the first paravertebral lung zone of the left upper lobe (Fig. 4-A). The films were seen by several phthisiologists and the consensus of opinion was that tuberculosis could not be excluded. Subsequent laminagraphic studies (Fig. 4-B) showed continuity of the previously demonstrated Y-shaped density with the left pulmonary artery at the hilum of the left lung. A roentgen diagnosis of anomaly of the superior branch of the left pulmonary artery was made. Pulmonary angiography was carried out using 70 per cent diodrast for opacification of the pulmonary arterial tree.* A roentgenogram of the chest, made three seconds after injection of the opaque substance, demonstrated the opacification of the shadow in the left upper lung field and simultaneous opacification of the pulmonary arteries. The angiogram confirms the laminagraphic impression of aneurysmal dilatation of a pulmonary artery.

Discussion: Full utilization of all anatomical structures, including fissures, bronchi, and vessels, is important in roentgen analysis of lobar and intralobar lesions. Many of these structures are best visualized by body section roentgenograms. The trachea and large lobe bronchi are always well visualized by this technic. The faint outline of third and fourth order bronchi may be inadequately seen even in good section films, but the images of the pulmonary arteries which closely parallel the bronchi are easily traced in serial layer films and are valuable landmarks of the intralobar segments of the lung. They can be most helpful in localization of pulmonary disease and in the interpretation of the results of the tuberculous process, which may give rise to exudation, ulceration, atelectasis, emphysema, and fibrosis.

Conclusions

Section roentgenography offers a simple technic for clear visualization of the anatomical thoracic structures that are important in clinical evaluation of tuberculous diseases of the trachea, bronchi, and lungs. It has made valuable contributions in roentgen interpretation of the tuberculous process and has aided in directing the clinical work-up of problem cases.

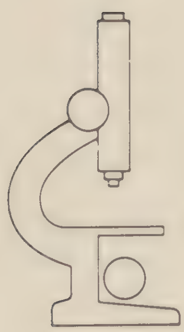
References

1 Grossman, G.: Lung tomography. Brit. J. Radiol., 1935, *8*, 733.

2 Kiefer, J.: The laminagraph and its variations: Application and implication of planigraphic study. Am. J. Roentgenol., 1938, *39*, 497.

* The angiogram was carried out by Dr. George P. Robb, who came to New Haven to demonstrate his technic of pulmonary angiography.

3 McDougall, J. B.: *Tomography*. H. K. Lewis and Co., Ltd., London, 1940.
4 McDougall, J. B., and Crawford, J. H.: Tomography with special reference to its value in the diagnosis of pulmonary lesions. Am. Rev. Tuberc., 1937, *36*, 163.
5 Moore, Sherwood: Body section radiography with the laminagraph. Am. Rev. Tuberc., 1938, *38*, 538-56.
6 Taylor, Henry K.: Planigraphic examination of the thorax in tuberculous individuals. Quart. Bull. Sea View Hosp., 1938, *3*, 357-74.
7 Wilson, H. M.: Exploration of the thorax by body section roentgenography. Radiology, 1939, *33*, 598.
8 Wilson, H. M.: Body Section Roentgenography. Cyclopedia of Medicine, Surgery, and Specialties; 1941, 640-48.
9 Young, B. R.: Value of body section roentgenography (planigraphy) for the demonstration of tumors, non-neoplastic disease, and foreign bodies in the neck and chest. Am. J. Roentgenol., 1942, *47*, 83.



notes

MINIMAL PULMONARY TUBERCULOSIS

DEMONSTRATION OF TUBERCLE BACILLI IN MINIMAL PULMONARY TUBERCULOSIS[1]

W. P. DECKER, W. H. ORDWAY AND E. M. MEDLAR

The importance given to the detection of pulmonary tuberculosis in the minimal stage of the disease is well known to all who are cognizant of the broad aims of the general tuberculosis program. It is also well understood that in the diagnosis of such cases fluoroscopic and roentgen-ray film examinations are a necessity, since very few patients exhibit any clinical manifestation of the disease in the early stages. Since the diagnosis rests almost wholly upon the observation of shadows in certain locations in the lung field, the demonstration of tubercle bacilli in the minimal cases is required to clinch the clinical diagnosis. This report presents the results obtained in this institution with the intensive use of the more thorough laboratory methods in the study of clinically active cases of minimal pulmonary tuberculosis. Such activity had as its essential requirement an unstable pulmonary lesion, as demonstrated by serial roentgen-ray films taken over a reasonable period of time.

There is little in the literature which deals directly with this problem. Stiehm (1) reported the demonstration of tubercle bacilli in 15 out of 21 cases of minimal disease. Barton (2) reports the finding of tubercle bacilli in 44 cases of minimal pulmonary tuberculosis as follows: by direct smear, 2; by smear of concentrate, 1; by culture, 8; and negative by all methods, 33. A recent report (3) from this institution indicated that tubercle bacilli were demonstrated in 27 out of 59 cases. Oyama (4) reported the demonstration of tubercle bacilli in 35 of 79 cases of primary infection and in one of the positive cases the X-ray film of the chest was normal; in 19 of 47 cases of pleural effusion; in 30 of 42 cases of early infiltration; and in 11 of 19 cases of apical tuberculosis. It is difficult to determine just how many of these cases would be classed as clinically active minimal pulmonary tuberculosis according to the National Tuberculosis Association standards. Kruger *et al.* (5) believe that it is unnecessary to try to demonstrate tubercle bacilli in the early cases prior to the institution of treatment, as the diagnosis is practically always obvious from the clinical and roentgenological examination of the patient.

The routine use of gastric lavage and of culture and guinea pig inoculation of concentrated specimens on all minimal cases was begun in this institution in 1936. Prior to that date only the patients who had expectoration were examined repeatedly by sputum concentrates and guinea pig inoculations if smears were negative. To compare the results of the laboratory studies two periods were selected: 1930–1935 and 1936–1941. It is generally recognized that persons in the early minimal stage often do not raise sputum. The proportion of "sputum" and "no sputum" cases for the two periods chosen are given in table 1.

It is to be noted that the ratio between "sputum" and "no sputum" cases is

[1] From the Metropolitan Life Insurance Company Sanatorium, Mount McGregor, New York.

practically the same for these two periods. In the first period only the "sputum" cases were studied for tubercle bacilli, while in the second period all the cases were adequately investigated by the more searching laboratory methods. The results of these studies for the two periods are given in table 2.

The marked increase of positive results shown in the second period demonstrates clearly the value of repeated examinations by culture and animal inoculation. This is further emphasized by the results obtained in the period 1939–1941, when even more through investigations were made, for during that period 92.9 per cent of the "sputum" and 80 per cent of the "no sputum" cases were proved to be positive. Throughout the study an especial effort was made to obtain an initial seventy-two-hour sputum or three consecutive facting gastric contents as soon as the patient was admitted. One-half of the cases in which tubercle bacilli were obtained were proved from this initial series of tests. If these initial tests were negative it was often necessary to make many tests

TABLE 1

Distribution of "sputum" and "no sputum" cases

PERIOD	NUMBER OF CASES	"SPUTUM"	"NO SPUTUM"
1930–1935	172	71 (41.3%)	101 (58.7%)
1936–1941	97	41 (42.2%)	56 (57.8%)

TABLE 2

Positive results obtained on "sputum" and "no sputum" cases of minimal pulmonary tuberculosis

PERIOD	NUMBER OF CASES	"SPUTUM"		"NO SPUTUM"	
		Number of cases	Per cent positive	Number of cases	Per cent positive
1930–1935	172	71	33.8	101	–
1936–1941	97	41	63.4	56	73.2

before bacilli were demonstrated. One example of this is a case in which bacilli were not demonstrated until the fifteenth series of gastric contents were examined.

Patients admitted to this institution come from all portions of the United States and Canada east of the Rocky Mountains. They may be classed into "Home Office" and "Field" regions. At the Home Office in New York City all employees have for years had yearly examinations which included fluoroscopy and, if deemed advisable, roentgen-ray films of the chest. Such has not been the general procedure in the Field. It is of interest then to compare the distribution of cases relative to the Home Office and the Field. These data are given in table 3.

In table 3 it will be noted that during the first period the ratio of "sputum" to "no sputum" cases was practically reversed in the two groups. During this period the "no sputum" cases were not investigated for the presence of tubercle

bacilli and in the "sputum" cases approximately the same percentage of positive results were obtained in the two groups. While the reverse ratio in "sputum" and "no sputum" cases in the two groups is not as great in the second period, it is still present. The change noted here may be due to the more general use of fluoroscopy and of roentgen-ray films in the detection of the early tuberculous case. It will also be noted that a considerably higher percentage of positive results was obtained in both groups due to the greater effort made to demonstrate tubercle bacilli. The reason for a higher percentage of positive results in the Home Office than in the Field group is not clear unless it can be ascribed to the earlier discovery of the lesion in a "fresh" exudative stage when bacilli may be more readily demonstrated.

A point of interest not shown in table 3 is the percentage of cases in which sputum smears were positive. For the period 1930–1941 29 per cent of the Home Office and 64 per cent of the Field group raised sputum. Positive smears were found in about the same percentage in the two groups, 12 per cent for the Home Office and 16 per cent for the Field. When the "no sputum" cases were included in each group, the Home Office group gave 3.5 per cent of positive smear cases while the Field gave 10.3 per cent of positive cases. Taking the groups as a whole, positive smears were found in 5.9 per cent of the cases. This is in marked contrast to the 69 per cent positive results obtained on all cases when a more thorough laboratory study was done during the period from 1936 to 1941.

TABLE 3

Distribution of cases on basis of "sputum" and "no sputum" with percentage of positive results obtained in "home office" and "field" groups

PERIOD	GROUP	TOTAL CASES	"SPUTUM"		"NO SPUTUM"	
			Number of cases and per cent	Per cent positive	Number of cases and per cent	Per cent positive
1930–1935	Home Office	111	29 (26)	34.5	82 (74)	–
	Field	61	42 (70)	33.3	19 (30)	–
1936–1941	Home Office	61	21 (35)	76.2	40 (65)	80
	Field	36	20 (55)	50.0	16 (45)	56.2

DISCUSSION

These studies have clearly demonstrated to us that there is a great variation, in cases of minimal pulmonary tuberculosis, in the number and frequency of discharge of tubercle bacilli. An occasional patient will discharge bacilli in such numbers that practically all smears of sputum examined will be positive, whereas another individual with a similar clinical and roentgenological picture will be found to discharge few bacilli on a rare occasion or not at all. From the pathogenesis of a tuberculous lesion one may postulate that, since the primary parenchymal tuberculous focus is but a small "open" area of bronchopneumonia,

all lesions of this type may discharge bacilli. It is not necessary to have demonstrable "cavity" formation prior to the discharge of bacilli from a tuberculous focus any more than it is necessary to have "cavity" formation before bacteria may be discharged from an early area of bronchopneumonia caused by streptococci or pneumococci. Kruger *et al.* (5) state: "At the same time we wish to stress the fact that a more recent analysis made by us of the frequency of bacillary sputum in noncavernous tuberculosis, even after adequate search, fails to confirm the high incidence of positive results reported by some observers." The acceptance of this statement depends entirely upon the interpretation of the words "sputum" and "adequate search." We believe that a high percentage of minimal tuberculous patients discharge a small amount of exudate from their bronchi but that in the majority of these cases the amount is so small that they are not conscious of "raising" anything from the lungs. This is the reason why it is necessary to obtain fasting gastric washings for study. If by "adequate search" is meant the examination of smears of "sputum" in the usually accepted sense, then it is agreed that only a small percentage of cases of minimal pulmonary tuberculosis will be found positive. In our group of 269 cases, in only 16 (5.9 per cent) was it possible to demonstrate tubercle bacilli in a smear of sputum. By the repeated use of cultures and guinea pig inoculations from concentrates of smear-negative sputum or of gastric washings we have increased the positive results from 5.9 to 69 per cent.

The following case clearly illustrates this discussion. Serial roentgenograms of the chest showed an unstable lesion. The patient discharged a small amount of purulent sputum daily. Numerous smears, both direct and of the sputum concentrate, failed to demonstrate tubercle bacilli. The individual was not clinically ill. Every culture of the sputum concentrate gave a fairly abundant growth of tubercle bacilli and every guinea pig inoculated developed tuberculosis. The private physician of this patient maintained that if it was so difficult to demonstrate tubercle bacilli such findings were of little consequence and it took many months of tactful persuasion before the patient was finally hospitalized. It required about a year of residence in the hospital before the sputum became intermittently negative by culture and guinea pig tests.

Since the use of repeated tests by culture and guinea pig inoculation on sputum and on gastric washings have been instituted, a high degree of corroboration of the clinical diagnosis of minimal pulmonary tuberculosis has been obtained. During the period 1939–1941 34 cases were studied and pathogenic tubercle bacilli were demonstrated in 29. There are two possible explanations for the failure to demonstrate the bacilli in 5 cases. First, the laboratory examinations may not have been made at the right time or in sufficient numbers. Second, there is a possibility that the lesion in these negative cases was not caused by the tubercle bacillus, for it is well known that other infections do occur in the pulmonary fields where tuberculous lesions are prone to develop. One may categorically state that the modern clinical diagnosis of minimal pulmonary tuberculosis has a very high percentage of accuracy. To regard the diagnosis as infallible is hardly the right attitude to assume. Perfection is rarely achieved in any branch of medicine.

Kruger *et al.* (5) advise the examination of repeated gastric contents and of sputum to determine whether, at the end of the course of treatment, tubercle bacilli are present. Stiehm (1) regards negative results after repeated tests as indicative of healing of the lesion. From the experience we have gained from our studies we wish to caution against placing too great emphasis upon a series of negative tests. In the first place, unless the presence and frequency of discharge of tubercle bacilli are determined at the time of discovery of the lesion or in the very early phases of treatment, then no yardstick is available to gauge the significance of a series of negative tests. Second, a series of such negative tests does not necessarily indicate a healed lesion. Two cases come to mind that illustrate these points. Two or three positive results were obtained shortly after these 2 patients entered the hospital and no further positive results were obtained from monthly tests during a period of two years. In one case the last specimen obtained proved to be positive after the patient was discharged and in the other case a positive result was obtained after the patient has returned to work. To date there has been no X-ray or clinical evidence of a relapse of the disease in these 2 cases. At the present time it is very difficult to determine when a minimal case of pulmonary tuberculosis ceases to discharge a few bacilli and to evaluate the significance of an occasional discharge of a few bacilli.

SUMMARY

Repeated examinations of sputum and of fasting gastric contents by culture and guinea pig inoculation have resulted in the demonstration of tubercle bacilli in 67 out of 97 patients with clinically active minimal pulmonary tuberculosis over a period of five years. In a previous five-year period, when the more thorough laboratory methods were not in routine use, tubercle bacilli were demonstrated in only 24 of 172 cases.

Gastric lavage studies gave positive results in 41 of 56 "no sputum" cases.

Sputum smears were positive in but 16 of 269 cases. This is no true indication of the number of patients who were discharging tubercle bacilli.

A very high percentage of clinically active minimal tuberculous patients discharge tubercle bacilli to a greater or lesser degree.

It is very difficult to determine when patients with minimal disease are entirely free from bacilli. It is just as difficult to evaluate the significance of the discharge of a few bacilli on rare occasions.

REFERENCES

(1) Stiehm, R. H.: Tubercle bacilli in the gastric contents: An important diagnostic and prognostic finding, Am. J. M. Sc., 1937, *194*, 340.

(2) Barton, R. M.: The importance of a standard of examination for tubercle bacilli, Indian M. Gaz., 1941, *76*, 598.

(3) Roper, W. H., and Ordway, W. H.: Gastric lavage in adults with pulmonary tuberculosis, Am. Rev. Tuberc., 1941, *43*, 543.

(4) Oyama, F.: Cultural demonstration of tubercle bacilli in gastric contents and its clinical significance, Tohoku J. Exper. Med., 1940–41, *39*, 505.

(5) Kruger, A. L., Potter, B. P., and Jaffin, A. E.: Management of the minimal tuberculous lesion, Am. Rev. Tuberc., 1942, *46*, 50.

FEATURES OF THE EARLY PULMONARY INFILTRATION

J. BURNS AMBERSON, Jr.[1]

The greatest obstacle to understanding the behavior of the earliest lesions of pulmonary tuberculosis is their failure to sicken the host. Access to the problem can be had only by a systematic study of groups of healthy people among whom, in time, the disease may be expected to appear. Since, next to absolute prevention of infection, identification and proper management of the early lesion is the most effective means of attack on tuberculosis, the importance of the study can easily be seen. Reports of various investigators have been published, most of which include observations of lesions by the X-ray, while they are still undetectable by other methods. At Bellevue Hospital a somewhat similar study has been under way for more than thirteen years, and the views which I am expressing here in a general way are based largely on this experience.

It has been variously stated that a person is unlikely to become a phthisic if he has passed the age of thirty or thirty-five without a demonstrable pulmonary lesion. If we except older people whose resistance has been depleted by uncontrolled diabetes, dietary deficiences, alcoholism, and the like, the statement holds. Furthermore, it is observed that the lesions of progressive pulmonary tuberculosis usually do not appear until after the start of adolescence. In other words, it is the span of life between adolescence and the early thirties which may be watched with the best prospect of detecting the first appearance of these lesions.

How quickly a lesion may appear in a lung which previously was healthy on X-ray examination is still not very clear. To answer this nearly accurately would require an X-ray examination of a group of healthy young people every week for a number of years; obviously, an objectionable undertaking. However, certain implications may be seen in our observations. For similar reasons we are not prepared to say much about the relation of the early lesion to recent primary infection. In contrast with young children a peculiarity in young white adults, who were tuberculin-negative, then became tuberculin-positive and still later developed pulmonary lesions, is the usual failure to demonstrate by X-ray a typical primary complex; visible enlargement of the regional lymph nodes usually is lacking. Consequently, because the frequency of tuberculin testing must be limited, it is seldom possible to judge clearly whether the lesion discovered is primary, or whether it represents an extension from the primary or an exogenous reinfection.

As to the pathological nature of the early lesion one must depend chiefly upon the interpretation of roentgenographic densities; and this must be done with considerable reservation. In a relative minority of instances the pulmonary field, which on previous examination was clear, contains a new, round, discrete, nodular shadow, usually less then a centimeter in diameter, which conforms with

[1] Bellevue Hospital, New York City.

that of a productive tubercle. But this appearance may be deceptive because it is known that the roentgenographic density of small exudative lesions at their start may have little of the collateral haze which is one of the signs of this type of reaction, that is, there may be a well defined border indicating the limitation of the inflammatory exudate within broncholobular walls rather than the periphery of a productive tubercle. The confusion is not so great in lesions more than a centimeter or so in diameter; first, because we know, the larger the size, the more likely is the process to be wholly or partly of an exudative lobular pneumonic nature, and second, because larger lesions usually cast shadows with soft hazy borders. At the autopsy of many chronic tuberculous subjects the reliability of these criteria is verified within certain limits by studying recent lesions of bronchogenic origin, the duration of which is fairly well known from antemortem observation. By this approach the conclusion is reached that most early lesions are predominantly exudative.

In practice one learns that age and race have an important influence. The younger the subject, the more likely is a newly developed lesion to be exudative, a feature which is somewhat more striking in adolescent girls than in boys, and in Negroes than whites. So many observations point this way that one is prompted to utter a dictum: Until careful observation proves otherwise, assume that a tuberculous lesion, newly developed in the lung of a previously healthy person, is an exudative infiltration and, therefore, potentially very unstable.

The term *infiltration*[2] is aptly applied to the exudative lobular pneumonic or bronchopneumonic lesion. Morphologically it has the same connotation now as it had when first used by Laennec to distinguish it from the tubercle. The distinction is fundamentally important because of the different potentialtities. Whatever the underlying cause may be, the productive (miliary or conglomerate) tubercle tends to follow a mild and indolent course, enlarging and undergoing caseation and excavation slowly, whereas the infiltration (gelatinous or gray) is much more labile, frequently spreading and breaking down rapidly. Similarly the infiltrate may become absorbed much more rapidly than the productive tubercle; or the serous and cellular elements at the periphery of the infiltrate may be absorbed while the liquefied caseous centre is excavated.

Sometimes, in retrospect, one may find in a previous roentgenogram a tiny focus which presumably may have been the precursor of the early infiltration, but, without a knowledge of subsequent events, the diagnosis of tubercle, rather than blood vessel, would have been highly imaginative, to say the least. Nevertheless, there is much to suggest that many or most recognizable early lesions are in reality extensions from preëxisting occult foci. What we call "early" applies only to that which is demonstrable. It is a relative term which once referred to the lesion initiating symptoms but now to that casting an identifiable roentgenographic shadow.

Knowing that exudative infiltrations inevitably change progressively or

[2] The term *infiltration* refers to the *process* by which the tissue is invaded by tuberculous inflammation, while the term *infiltrate* is used to indicate the lesion produced by the process.

retrogressively, we have paid particular attention to the later evolution of those discovered early. The dominant trend of extensive pneumonic infiltrations to caseation and excavation has been noted by clinicians generally. Small early infiltrations behave in a similar way, the one apparent difference being quantitative; central necrosis is the striking tendency. In fact, this is so common as to suggest that almost all, if not all, early lesions are caseous at the centre by the time they can be diagnosed by X-ray. The cavity, when present, is often so minute that it can scarcely be recognized in the roentgenogram; special techniques may be required. That the pinhead or pea-sized rarefactions usually denote excavation is verified by their later enlargement and, as a rule, by the demonstration of tubercle bacilli in the scanty sputum or in the gastric washings upon meticulous examination.

The behavior of the periphery of the early infiltration is conditioned largely upon the rate and extent of the central caseation, the apparent reason being that the former depends upon the rate of manufacture in and local diffusion of toxic substances from the latter. If caseation is minimal and sloughs out early, the peripheral exudate is likely to be absorbed rapidly, and the minute cavity may close promptly; secondary bronchogenic lesions are slight or absent. If caseation is rapid and extensive, peripheral extension is greater; when the liquefied matter is discharged into the bronchial tubes extensive—even lobar pneumonic—secondary lesions may result. If caseation is small or moderate in extent (usually not more than 1 or 2 cm. in cross-section) and becomes arrested with little or no ulceration into the bronchus, the peripheral exudate may be gradually absorbed and organized, encapsulating the cheesy residues; roentgenographically, these often have the appearance of so-called "round infiltrates."

The rate and succession of these changes vary greatly. At the start of our study the usual routine of making roentgenographic observations once a month or so was followed. Soon it was found that some lesions changed markedly in this interval. Now it is routine, upon discovering a newly developed lesion in a previously healthy person, to make the examination every week during the first one or two months. Occasionally an interval of several days is the limit. It has been discovered, especially in adolescent and young adult patients, that a cavity, 2 or 3 mm. in diameter, may appear within a week; an infiltration 1 cm. in diameter may double or triple its size in one to four weeks; an infiltration 1 to 2 cm. in diameter may abruptly discharge its liquefied caseous contents into the bronchi, thus inciting an acute tuberculous lobar pneumonia within two to four weeks. Some early infiltrations remain stationary for weeks or months, then rapidly change with excavation and numerous and extensive secondary lesions. The transition from the early lesion to advanced bilateral disease, in exceptional cases, is a matter of only a few weeks. Resolution, when it occurs, is slow. At first the peripheral exudate, perhaps quite serous, may be seen to absorb rapidly within several weeks, but as a rule the process slows as the core of the lesion is approached. In several months minute residues remain—almost naked caseous remnants which may be visualized as collections of myriad or-

ganisms, delicately imprisoned, waiting for some passing disturbance to spread them far and wide. Needless to state, the warm, fertile lung is ever receptive for the threatened dissemination. During the subsequent two years, approximately, circumstances decide whether wide destruction is initiated, whether the slow process of fibrous encapsulation may become competent and permanent, or whether an indecisive balance between the forces of destruction and repair leaves the lesions in that uncertain and sad state, known as chronicity.

For the clinician especially a most interesting observation is the lag between pathological morphological change and systemic effects. For example, upon first discovering an early infiltration the erythrocyte sedimentation rate usually is reported normal. During the subsequent few weeks a steady or intermittent extension of the lesion, perhaps with excavation, may occur without any coincidental change in this test. Then as the pulmonary involvement continues the sedimentation rate for the first time is accelerated; a few days or weeks later the initial fever may be detected. One may interpret this to mean that the diffusion of toxins must persist and reach a considerable level before the systemic effects are measurable by the ordinary clinical and laboratory tests. In some cases tubercle bacilli are discovered in the sputum before these effects are detected.

Certain implications may be seen in these observations. In all probability a tuberculous infiltration may develop in the lung within a few days to several weeks. That this may be the first demonstrable extension from a preëxisting occult focus cannot be denied.

When an infiltration is fresh, with only minimal central caseation, the possibility of resolution and complete healing is greater than it is at any subsequent phase of the disease. Conceivably, conditions would be more favorable if the small caseous core had been extruded, but this seldom occurs without some infection of the surrounding parenchyma.

The opportune time for securing maximal effects of treatment is in this early phase, preferably before there are any severe systemic symptoms and before secondary bronchogenic lesions have had time to develop. To wait for the lesion to give indubitable evidence of its "activity" usually means that the best opportunity for cure has been lost. Fortunately, this does not imply that an "arrestment" may not occur later. But, to accomplish the most for the patient, the fact must frequently be emphasized and well remembered that a small lesion, demonstrable only by X-ray and wholly symptomless, may be an early infiltration with serious and closely impending potentialities. Unless it is unmistakably fibroid, such small lesions at the start should be observed roentgenographically at weekly to biweekly intervals. Preferably, the patient should be on rest treatment while this is done. These conceptions have proved in our experience to be a sound basis of treatment with results surpassing any other scheme which we have tried. The experience seems to indicate that, if the conceptions could be applied generally, tuberculosis would seldom become the advanced and fatal disease with which, regrettably, we are so familiar.

SUMMARY

The behavior of the earliest lesions of pulmonary tuberculosis can be understood only by a systematic study of apparently healthy people among whom the disease may be expected to appear. The period of life between the start of adolescence and the age of thirty or thirty-five is the time during which most of these lesions first develop.

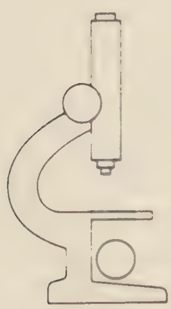
Most lesions of the early infiltration are of a predominantly exudative, lobular pneumonic character; this type of tissue reaction is most conspicuous in adolescents, especially in young girls and in Negroes. The assumption should be made, until well proved otherwise, that this type of reaction prevails, remembering that the roentgenographic appearance may be misleading.

The striking tendency of the early infiltration is to progress to the point of caseation and excavation. Close study demonstrates that such changes may be rapid; for example, a small lesion may enlarge, caseate, and slough out within a week or two, and given rise to extensive secondary bronchogenic lesions.

Usually, systemic effects, such as fever and an accelerated erythrocyte sedimentation rate, are not apparent at the time of the early infiltration and there is often a considerable lag in these effects while the lesion is advancing.

It may be inferred from our studies that the early infiltration may develop within a few days or weeks in the lung of a previously healthy person. There is reason to believe that in many or most instances there have been preëxisting occult foci which served as points of origin.

Treatment is most successful if it is based on these conceptions; usually advanced tuberculosis can be avoided.



ACCIDENTALLY DISCOVERED PULMONARY TUBERCULOSIS[1]

HANS ABELES AND MAX PINNER

With draft examinations, X-ray surveys in industry and colleges and many other roentgenological surveys of apparently healthy persons, thousands of persons with X-ray evidence of pulmonary tuberculosis are discovered who have no symptoms of disease that induced them to ask for medical advice. In a certain percentage of these "accidentally discovered" cases, the film permits the unequivocal diagnosis of active pulmonary tuberculosis (with slim chances of an occasional nontuberculous disease simulating tuberculosis); in another portion of these cases, the first film justifies the assumption—which must be proven—that the lesions seen are healed or arrested. But in a considerable percentage the diagnosis of activity is neither readily made nor excluded.

The great medical, social and financial importance of the decision "active or nonactive" is obvious and is further emphasized by the difficulty and frequent uncertainty of the decision.

In the past, a number of "single-test" activity diagnoses were advocated, tried and found wanting. In this category belong, in our opinion, all serological, blood-chemical and haematological tests for activity. They are nonspecific and are, therefore, sometimes positive in the absence of active tuberculosis and they are not sensitive enough to detect all active cases.

In the past few years, we have observed 91 patients in our Sanatorium whose tuberculosis was discovered accidentally. No special tests were applied to these patients, but they were observed in a routine way, stressing all those observations which seemed likely to answer the question "active or nonactive." Since a retrospective evaluation of certain criteria for activity yielded clear-cut results, their publication seemed justified.

Sex and age of the patients: Sex and age distribution of the patients are presented in table 1. These figures are not likely to be representative because selected age groups of healthy persons are more frequently examined than others.

Reason for examination: The reasons for examination were as follows:

Selective service examination	29 cases
Examined as contact case	25 cases
Preëmployment examination	14 cases
School survey	8 cases
Hospital employees (routine examinations)	6 cases
Various reasons	9 cases

In the group of "various reasons" fall patients diagnosed on the occasion of free examination of union members, of premarital examination etc.

History of contact: Twenty-five patients were originally examined as contact cases. In another 13 patients, a definite history of contact could be elicited.

[1] From the Country Sanatorium, in Bedford Hills, New York, of the Montefiore Hospital for Chronic Diseases, New York City.

"Definite contact" includes those patients who lived with, or met frequently, or had professional contact with a known tuberculous person for a long period of time. In 8 patients there was a questionable history of contact. The time elapsed between the break of contact with the known tuberculous person and the diagnosis in the cases with definite contact-history is given in table 2. Fifty per cent of all cases with a definite history of contact were diagnosed within six months after the contact had been broken. Home contact was found in 29 cases, close contact with the probable source of infection but no common household was found in 3 cases. Professional contact—physicians, nurses, attendants on tuberculosis wards—was present in 6 cases.

Symptomatology: Since the patients were discovered on routine examinations, one might expect to find a large number of asymptomatic cases. However, in

TABLE 1

Sex and age of patients

	AGE IN YEARS					TOTAL
	10–19	20–29	30–39	40–49	50–59	
Number of patients						
male	10	29	15	8	2	64
female	8	17	1	0	1	27
Total	18	46	16	8	3	91

TABLE 2

Time interval between break of contact and diagnosis

TIME INTERVAL	NUMBER OF CASES
Less than 6 months	19
Between 6 months and 1 year	4
Between 1 year and 2 years	4
Between 2 years and 3 years	5
Between 3 years and 5 years	1
Over 5 years	5

many cases a carefully taken history revealed definite symptoms. According to symptoms the patients were divided in the following groups:

No symptoms at any time	16 patients
Symptoms on retrospect	1 patient
Symptoms prior to or at the time of the diagnosis	58 patients
Symptoms at any time after establishment of the diagnosis	16 patients

Sixteen patients never had any symptoms referable to their pulmonary disease. Five of the 16 patients never presented any evidence of active disease. The findings in the active, asymptomatic cases are presented in table 3. Practically all stages of tuberculous lesions, from a small exudative lesion to far advanced fibrocavernous disease, were found in the group of asymptomatic patients.

TABLE 3

Asymptomatic patients with active disease

CASE NUMBER	REASON FOR EXAMINATION	PREVIOUS NORMAL X-RAY	X-RAY FINDINGS	PHYSICAL EXAMINATION	STAGE	BACTERIOLOGICAL FINDINGS	ESR	WBC	COURSE
33	Hospital employee	2 months prior	Early infiltrate RUL	Normal	Minimal	Negative	10	10,050	Discharged arrested
81	Selective Service	None	Productive infiltrate BUL	Normal	Minimal	Negative	5	9,000	Discharged arrested
88	Selective Service	1 year prior	Productive infiltrate RUL	Normal	Minimal	Negative	2	9,000	Discharged arrested
10	Contact	12 months prior	Exudative infiltrate RUL	Normal	Moderately advanced	Positive gastric concentrate	9	10,500	Progression, pneumothorax
18	Selective Service	None	Productive cavitary lesions BUL	Normal	Moderately advanced	Positive gastric concentrate	5	10,600	Died postoperative
46	Union survey	None	Exudative infiltrate RUL	Râles RUL	Moderately advanced	Negative	28	10,000	Discharged arrested
64	Contact	None	Productive infiltrate RUL	Normal	Moderately advanced	Positive gastric culture	4	8,500	Discharged arrested
66	Selective Service	None	Productive infiltrate RUL	Normal	Moderately advanced	Positive gastric culture	7	13,200	Discharged arrested
78	Selective Service	None	Productive cavitary lesions BUL	Râles BUL	Moderately advanced	Positive gastric concentrate	12	9,350	Progression
11	Contact	2 years prior	Exudative cavitary lesions RUL	Normal	Far advanced	Positive gastric concentrate	20	6,800	Pneumothorax, arrested
80	Selective Service	None	Productive infiltrate BUL	Râles BUL	Far advanced	Positive gastric culture	24	9,900	Discharged arrested

This shows that no characteristic correlation existed between the absence of symptoms and the extent or type of the disease.

Fifty-eight patients, that is, 67.4 per cent of all active cases, had symptoms prior to or at the time of diagnosis. Symptoms were often disregarded even when they were as obvious as small haemoptyses because the patients felt well otherwise, or they were ascribed to other conditions, such as nose bleeding, overwork, mental strain etc. Only one patient had symptoms on retrospect. This patient was a resident on pathology when a minimal infiltration was noted on a routine chest film. He had had a normal X-ray film six months prior to the diagnosis. Patient emphasized that he had no symptoms. However, after several months of bed-rest, he volunteered the statement that he felt better, that is, he now felt really rested.

Sixteen patients developed the first symptom after the diagnosis had been made, some of them as late as two years afterwards. Symptoms due to therapeutic measures or complications of the treatment were not included in this group.

TABLE 4

Time interval between onset of first symptom and diagnosis

TIME INTERVAL	NUMBER OF CASES
More than 3 years prior to the diagnosis	3
Between 3 and 2 years prior to the diagnosis	2
Between 2 and 1 years prior to the diagnosis	2
Between 1 year and 6 months prior to the diagnosis	12
Within 6 months prior to the diagnosis	27
At the time of diagnosis	12
Within 6 months after the diagnosis	6
Within 1 year after the diagnosis	4
Within 2 years after the diagnosis	7

The time elapsed between the onset of the first symptom and the diagnosis is presented in table 4. The 3 patients who had symptoms more than three years prior to the diagnosis had small haemoptyses at that time. When diagnosed, all 3 patients had cavitary lesions. The period in which most cases developed the first symptom was from one year prior to the diagnosis up to the time of diagnosis; 52 patients (this includes the patient with symptoms on retrospect), or 69.3 per cent of all patients with symptoms, developed them within this time interval.

The frequency of the symptoms encountered as first ones is presented in table 5. If, as it happened in many cases, more than one symptom was noticed at approximately the same time each symptom was entered in the corresponding line. The high incidence of fatigue—an easily misinterpreted symptom—as first symptom is probably one of the reasons that the patients did not seek medical advice any sooner.

Physical and roentgenological findings: Definite findings on physical examination indicating pulmonary disease were found in 35 patients. Slight dulness

and minimal changes of breath sounds were not considered as definite pathological findings and, therefore, were not included in this group.

At the time of diagnosis, 28 patients had minimal, 40 moderately advanced and 23 far advanced disease. The large number of far advanced cases is remarkable.

According to roentgenological findings, 47 patients had bilateral lesions; in 31 only the right lung and in 13 only the left lung was involved. Fifty-five patients had a mainly productive type of infiltration, 33 a mainly exudative type and 3 a productive type with a recent exudative spread. In 17 patients the

TABLE 5

Incidence of first symptoms

SYMPTOM	NUMBER OF CASES
Fatigue	36
Cough	32
Sputum	24
Weight loss	15
Cold, grippe	12
Pain	11
Streaking, haemoptysis	9
Night sweats	6
Loss of appetite	1

TABLE 6

Location and extent of lesions

LOCATION	RIGHT LUNG	LEFT LUNG
Apical and subapical region	8	11
First anterior intercostal space	7	5
Between first and third anterior rib	12	9
Between first and fourth anterior rib	5	3
Between apex and third anterior rib	35	25
Between apex and fifth anterior rib	11	7
	78	60

characteristic distribution of haematogenous seeding was seen. Seven patients had an early infiltrate and one had a large pneumonic infiltration. Sixteen patients had a definite cavity at the time of diagnosis; in all these 16, tubercle bacilli were demonstrated on smear or concentration. In 13 additional patients, a diagnosis of a possibly cavitary lesion was made when they were first seen. In 10 of these 13 patients, tubercle bacilli were found on smear or concentration, in 3 by sputum or gastric cultures. In 9 of the 13 patients with possibly cavitary lesions, tomograms were taken which confirmed the diagnosis in 4 cases.

The location of the lesions is shown in table 6. Seventeen patients had an X-ray film taken previously which was normal; 10 a year or less, 4 one to two

years, 3 over two years prior to the diagnosis. Of the 10 cases which had normal X-ray findings one year or less prior to the diagnosis, 6 were classified as minimal, 3 as moderately advanced and one as far advanced. In 6 of the 10 patients, tubercle bacilli were demonstrated in the sputum or gastric content. In 7 the lesion was exudative, in 3 productive; in 2 cases a cavity was found when diagnosed.

Laboratory findings: Sputa were examined on direct smear, concentration and by culture. If no positive findings were obtained by these methods the gastric content was examined on concentration and by culture. In many patients bacilli were demonstrated only after repeated negative results. Tubercle bacilli were recovered from 77 patients, or 84.6 per cent of all cases. The detailed results are presented in table 7. In 14 cases, no tubercle bacilli could be demonstrated by the above mentioned methods at any time.

Five of the 14 cases with entirely negative bacteriological findings were, after prolonged clinical and roentgenological observations, considered inactive. The findings in the consistently negative, active cases are presented in table 8. Of these active cases, 6 had minimal lesions and 3 had moderately advanced disease.

TABLE 7

Result of bacteriological examinations

TOTAL NUMBER OF CASES	ACTIVE CASES	POSITIVE BACTERIOLOGICAL FINDINGS	POSITIVE SPUTUM			POSITIVE GASTRIC	
			Smear	Concentrate	Culture	Concentrate	Culture
91	86	77	19	26	4	8	20

A white cell count above 10,000 was found in 37 patients. A sedimentation rate above 9 mm. per hour, Westergren method, was present in 54 patients.

Activity of lesions: Whether or not a lesion is active was frequently decided only after months of observation. In most patients, the diagnosis of activity is based on more than one single criterion.

In our routine observations for activity, frequent X-ray and bacteriological examinations were done, supplemented by complete blood counts and sedimentation rates (Westergren method). Those data, combined with careful observations of symptoms, extended over a minimum period of six months, formed the basis for the final decision as to activity of the lesions. The most convincing indications of existing activity were changes—progressive or retrogressive—in serial X-ray films and demonstration of tubercle bacilli.

Table 9 shows which of the above criteria were positive in the 86 cases which were finally judged to be active.

In table 10 these findings are correlated with the stage of the disease. From these tables it can be seen that roentgenological changes, positive bacteriological findings and symptoms are the criteria most frequently present in active cases. In 87.2 to 90.7 per cent they established the diagnosis of an active lesion, while

TABLE 8

Active cases with negative bacteriological findings

CASE NUMBER	REASON FOR EXAMINATION	PREVIOUS NORMAL X-RAY	X-RAY FINDING	PHYSICAL EXAMINATION	SYMPTOMS	STAGE	ESR	WBC	CRITERIA OF ACTIVITY	COURSE
33	Hospital employee	2 months prior	Early infiltrate RUL	Normal	None	Minimal	10	10,050	X-ray findings, WBC? ESR?	Discharged arrested
35	Hospital employee	6 months prior	Productive infiltrate BUL	Normal	Productive cough	Minimal	20	8,000	X-ray findings, symptoms, ESR	Discharged arrested
44	Hospital employee	1 year prior	Early infiltrate LUL	Normal	Pain, cough	Minimal	12	9,800	X-ray findings, symptoms, ESR	Discharged arrested
81	Selective Service	None	Productive infiltrate BUL	Normal	None	Minimal	5	9,000	X-ray findings	Discharged arrested
83	Selective Service	None	Productive infiltrate RUL	Normal	Fatigue	Minimal	10	11,200	X-ray findings, symptoms WBC, ESR?	Lesions unstable
88	Selective Service	1 year prior	Productive infiltrate RUL	Normal	None	Minimal	2	9,000	X-ray findings	Discharged arrested
46	Union survey	None	Exudative infiltrate RUL	Râles RUL	None	Moderately advanced	28	10,000	X-ray findings, ESR, physical examination	Discharged arrested
87	Contact	None	Exudative infiltrate BUL	Râles RUL	Weight loss	Moderately advanced	10	8,900	X-ray findings, symptoms, ESR? physical examination	Readmitted after 9 months
91	Selective Service	None	Productive infiltrate, BUL	Normal	Weight loss	Moderately advanced	32	11,100	X-ray findings, symptoms, ESR, WBC	Discharged arrested

sedimentation rate, white cell count, physical examination were reliable in only 40.7 to 62.8 per cent.

Of the entire group of 91 patients, 5 were considered to have inactive disease. The latter were observed for at least six months with the exception of one case which was observed for four months. In several inactive cases the negative bacteriological findings were confirmed by guinea pig inoculation. The findings

TABLE 9

Basis for the diagnosis of activity of the disease

BASIS FOR THE DIAGNOSIS OF ACTIVITY		NUMBER OF CASES	PERCENTAGE OF ACTIVE CASES
X-ray findings clearing	31	78	91
progression	34		
cavitation*	13		
Bacteriological findings		77	90
Symptoms		75	87
Sedimentation rate		54	63
White blood count		37	43
Physical examination		35	41

* In these cases no comparison X-ray was available since pneumothorax was induced shortly after the first film had been taken.

TABLE 10

STAGE	NUMBER AND PER CENT OF CASES	ACTIVE CASES	X-RAY SIGNS OF ACTIVITY	ACTIVE CASES					
				Positive bacteriological findings	Symptoms at any time	Elevated ESR	Leucocytosis	Progressive lesions	Collapse therapy
Minimal	28 31%	26 93%	26 100%	20 77%	23 89%	18 69%	9 35%	14 54%	9 35%
Moderately advanced	40 44%	38 95%	34 90%	35 92%	32 84%	20 53%	16 42%	15 40%	13 34%
Far advanced	23 25%	22 96%	18 82%	22 100%	20 91%	16 73%	12 55%	5 23%	13 59%
Total	91	86 100%	78 91%	77 90%	75 87%	54 63%	37 43%	34 40%	35 41%

in the inactive cases are tabulated in table 11. In all of them sedimentation rate and white cell count were normal. Although differential white cell counts were done in all patients, criteria of activity derived from them were not considered, because former studies had convinced us that they are more frequently unreliable in active cases than the criteria used in this study.

Course and therapy: Of the 86 patients with active disease, 34 were active progressive, that is, they showed definite progression on serial X-ray films. Of the

86 patients suffering from active disease, 51 were treated conservatively; 35 patients were subjected to collapse therapy—33 are receiving pneumothorax treatment, 5 of them bilaterally, and 2 underwent thoracoplasty. Two patients died; one death occurred postoperatively following a thoracoplasty. The other death occurred in a hospital employee in whom a minimal lesion was found on routine examination one year after a normal X-ray film had been obtained. This patient refused treatment when diagnosed. Within a year the symptoms became so severe that he sought hospital care and at that time the disease was far advanced and cavitary. The patient died of caseo-cavernous tuberculosis three years after the diagnosis had been made. Although many cases have been followed for several years, others have been under observation for six months only. No final conclusion as to the course and prognosis can therefore be drawn. However, even the incomplete follow-up reports bring out certain factors so

TABLE 11

Inactive cases

CASE NUMBER	REASON FOR EXAMINATION	X-RAY FINDING	PHYSICAL EXAMINATION	STAGE	ESR	WBS
52	Selective Service	Productive infiltration LUL	Normal	Minimal	5	8,500
82	Selective Service	Productive infiltration RUL	Normal	Minimal	5	8,500
75	Selective Service	Productive infiltration BUL	Normal	Moderately advanced	5	8,700
85	Selective Service	Fibro-calcific infiltration BUL	Normal	Moderately advanced	9	9,200
51	Selective Service	Fibro-calcific infiltration BUL	Normal	Far advanced	1	9,050

clearly that it seems worth while to report them: 41 patients have been discharged; 7 patients who had cured at our institution were readmitted to our or another institution; 9 patients who had cured at another institution were admitted to our institution. The time interval between discharge and readmission varied from one month to three and a half years with an average of twelve months per case. The immediate reasons for readmission were as follows:

Progressive X-ray changes	6 cases
Progressive X-ray changes and symptoms	3 cases
Progressive X-ray changes and positive sputum	2 cases
Haemorrhage	2 cases
Positive sputum on concentration	2 cases
Progressive X-ray changes, symptoms and positive sputum	1 case

No tubercle bacilli could be demonstrated in 6 of the 16 readmitted cases at the time of the first admission. During the course of the second admission,

tubercle bacilli were found in the sputum or gastric contents of all 16 patients with the exception of one who had a moderately advanced lesion which was definitely unstable as demonstrated by X-ray changes. All inactive cases were discharged at least half a year ago. They are working and none of them have shown signs of an active lesion since.

COMMENT

The results of this study are obvious and simple; how generally applicable they are remains to be determined in much larger series of patients. It must be pointed out that our patients represent a selected material: they were sent to the Sanatorium because some physicians thought they needed treatment, that is, they considered them active. This selection was well done, since only 5 out of 91 patients were finally judged not to have shown any evidence of activity. We do not know how this selection was made, but we have reasons to believe that mainly roentgenological criteria were used, supplemented in many cases by bacteriological findings.

On the other hand, it is impossible to know how many persons with radiological findings were not hospitalized because it was believed that they had no activity, but who actually were active. In order to gain a well rounded picture, it would be necessary to study a large unselected group of persons with abnormal radiographic findings and study them as intensively as the patients described in this study.

It is reassuring to find, quite in accordance with fairly well established clinical practice, that three criteria for activity—radiographic instability, properly related symptoms and bacterial findings—have a high degree of reliability; that is, they all are positive in about 90 per cent of active cases.

In contrast to this, the sedimentation rate, which is still being recommended as a trustworthy indicator of activity, failed in about 40 per cent; leucocytosis and physical examination correctly suggested activity in less than half of the active cases.

The customary warning regarding sputum examination so frequently goes unheeded that it must be repeated: Negative bacteriological findings are significant only if based on numerically sufficient and technically adequate examinations. As shown in table 7, 24 of 77 positive findings were obtained only by culture (and frequently not by the first culture made); 28 of the positive findings depended on examination of gastric contents. It is quite possible that the results could be improved by systematic use of animal inoculation.

It should be pointed out that even in minimal active cases bacilli were found in nearly 80 per cent. The significance of positive bacillary findings is here stressed entirely from the point of view of diagnosing activity and not from that of prognosis and treatment which is still a much more debatable question.

It has become customary to call all accidentally discovered patients with pulmonary tuberculosis asymptomatic cases. The silent assumption that the symptomatic patient will ask for examination is incorrect. The care with which the patient is questioned (not only at the time his lesion is discovered but later on

after mental resistance against acceptance of the diagnosis has been softened and after he has become more familiar with the subjective manifestations of the disease) will determine to a large degree how many of these patients are really asymptomatic. In our selected series, only 16 of 86 active patients never complained of any symptoms. But careful attention to symptoms is, of course, much easier in a Sanatorium than in a follow-up clinic.

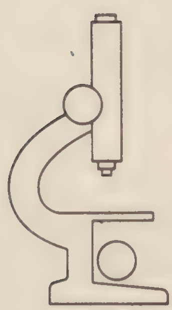
SUMMARY

1. Ninety-one cases of accidentally discovered pulmonary tuberculosis were investigated.

2. At the time of diagnosis 30.7 per cent of all cases had minimal, 44 per cent moderately advanced and 25.3 per cent far advanced involvement.

3. Of the 91 cases, 94.5 per cent had active disease; 39.5 per cent of them had active progressive disease.

4. In the 86 cases with active disease, serial X-ray changes were observed in 90.7 per cent, tubercle bacilli were demonstrated in 89.5 per cent and 87.2 per cent had symptoms referable to their pulmonary tuberculosis. In contrast to this, the sedimentation rate was elevated in only 62.8 per cent and the total white cell count was above normal in only 43 per cent of the active cases.



THE SERIOUSNESS OF MINIMAL PULMONARY TUBERCULOSIS[1]

S. C. STEIN AND HAROLD L. ISRAEL

The outlook for patients with minimal tuberculosis, when contrasted with the outlook for patients with advanced tuberculosis, has appeared so favorable that it has seemed almost sufficient to make an "early" diagnosis to ensure a satisfactory result. This belief has been based largely on reports of the benign course of minimal tuberculosis observed in patients in sanatoria, such as at Trudeau Sanatorium, where a fatality rate of only 2 per cent was noted in patients with minimal disease after six years' observation (1). It is the purpose of this report to point out that sanatorium patients comprise a selected group and that observations on the course of minimal tuberculosis in members of this group are not applicable to the problem in the population at large.

Studies at the Henry Phipps Institute of the course of minimal tuberculosis have shown widely divergent results in different groups. Observation of a group of 16 students, found to have asymptomatic minimal tuberculosis in a survey of a municipal teachers' training college, revealed that 5, or 31.1 per cent, had died within six years (2). Among clinic patients diagnosed as having clinically manifest minimal tuberculosis at the Henry Phipps Institute between 1932 and 1937, fatality rates of 9.1 per cent in whites and 15.0 per cent in Negroes were found after a somewhat shorter average interval of observation (3). Observation of medical students (4) and student nurses (5) with minimal tuberculosis has shown an extremely low fatality rate; in both these groups, however, roentgenological and clinical progression have been frequently noted.

It is obvious that to a considerable extent the differences in course exhibited by sanatorium patients and by clinic patients and professional groups are the result of the social and economic differences among these groups. In addition, however, the prognosis in minimal tuberculosis depends upon whether the lesion is of an acutely progressive type or of a chronic, slowly progressive type. If previous X-ray films are available, it may be possible to determine accurately whether the lesion is of recent origin. In most instances, prior films are not available, and estimates as to the duration and character of the disease must be based on the roentgenological appearance of the lesion or upon the length of illness reported by the patient. Unfortunately, judgments as to the age of a lesion based on roentgenological appearance are frequently in error, and only a small minority of patients with minimal tuberculosis have symptoms. It is because of these difficulties that paradoxically the prognosis is in general better in patients with symptomatic minimal tuberculosis than in those with asymptomatic disease. The very fact that after several months of ill health a lesion has not advanced beyond the minimal stage indicates that the process is a proliferative, slowly progressive one. There can be no such presumption of chronicity in asymptomatic disease: minimal tuberculosis detected in the asymptomatic phase actually represents a cross-section of potentialities. Some of the lesions

[1] From the Henry Phipps Institute of the University of Pennsylvania, Philadelphia.

may be stable, some may be retrogressive, some slowly progressive and some, as in the following case, acutely progressive.

R. D., an Italian female, aged fifteen, was examined in 1934, as an apparently healthy contact of a tuberculous sister. The tuberculin reaction was positive. X-ray examination at the time of the initial visit was negative, as were periodic films made at three to eight month intervals because of recurrent exposure. In December, 1937 the presence of a faint apical infiltration was suspected. A definite patch of flocculent infiltration was visible on reëxamination four months later. Although there were no symptoms or physical signs and although the sedimentation rate was normal, sanatorium treatment was advised, application for admission was made and the patient was instructed to stop work and to rest at home. The patient was reëxamined one month later when her call to the sanatorium was received. There had been a nine pound weight gain, and there were no symptoms, but X-ray examination revealed the development of a cavity 2 cm. in diameter. The patient was given the routine rest treatment at the sanatorium. It was not until four months later that respiratory symptoms developed and positive sputum was obtained. Pneumothorax treatment was refused and the patient died of tuberculosis in April, 1939.

This case is not only an instance of rapidly progressive tuberculosis occurring in the asymptomatic phase, but serves also to point out another factor responsible for the divergent results seen in sanatoria and in clinics. This patient represented to the clinic a fatal termination of minimal tuberculosis; to the sanatorium, however, she represented the fatal end of a case of moderately advanced disease. It is quite the rule for weeks and even months to elapse before admission to a sanitorium is effected. Patients found to have asymptomatic minimal tuberculosis, when examined in a survey or in a clinic, not uncommonly have had progression of disease by the time they are admitted to the sanatorium. Frequently patients with asymptomatic minimal lesions will refuse institutional care until symptoms appear as the result of cavity development.

It appears correct, therefore, to consider those patients who enter sanatoria with minimal lesions as a selected group, not comparable to the total of patients found with minimal tuberculosis in clinics and in surveys. Many patients in the latter group, by constitution or by circumstances, are less well favored in that they may have a greater proportion of acutely progressive lesions, a lesser opportunity for speedy sanatorium admission or a poorer psychological or sociological ability to accept immediate sanatorium care, if such opportunity exists.

The present program of mass X-ray examination is directed principally at those groups in which tuberculosis presents the most serious problem: contacts of known cases, industrial workers, the unemployed. It would be a mistake to base the management of cases of minimal tuberculosis found in such surveys on expectations derived from the course of the disease as observed in sanatorium patients. It would be much more reasonable to base treatment on the course observed in the other groups of the population. Table 1 has been prepared to show the outcome of disease in 66 consecutive patients with minimal tuberculosis, diagnosed at the Henry Phipps Institute between 1937 and 1940, concerning whose status information was available a year after diagnosis. This number

does not include the large group of patients whose lesions were obviously or apparently healed; only those patients whose X-ray shadows appeared to the roentgenologist sufficiently flocculent or extensive to warrant consideration of treatment are included. The lesions were in most instances asymptomatic.

The frequency with which progression, often fatal, occurred is especially significant in view of the relatively short period of observation. As suggested by the case history given above, progression occurred in some cases despite relatively prompt application of therapy. In other cases, progression presumably occurred because of failure to follow the recommendations of the staff conference. In a number of cases, however, progression probably resulted from the failure of the staff conference to advise proper treatment. Although the serious potentialities of asymptomatic minimal tuberculosis have long been recognized and emphasized at the Henry Phipps Institute, inability to distinguish, roentgenologically, fresh from chronic lesions frequently results, especially in older patients, in the recommendation of observation instead of the immediate application of treatment.

TABLE 1

The results of observation of clinic patients with minimal tuberculosis*

	NUMBER OF PATIENTS	DISEASE STABLE OR RETRO-GRESSIVE	INDETERMINATE RESULT	DISEASE PROGRESSIVE	
				Alive	Dead
White	16	8 (50%)	2 (13%)	5 (31%)	1 (6%)
Negro	50	24 (48%)	2 (4%)	13 (26%)	11 (22%)

* The period of observation ranged from one to five years; the mean duration was 30.8 months.

It is evident that the present vigorous campaign for detection of minimal tuberculosis by roentgen-ray examination of large groups of the population will avail but little if mere observation or only brief periods of treatment are given patients with such lesions. It is necessary that the serious potentialities of asymptomatic minimal tuberculosis be recognized, that adequate sanatorium facilities be provided and that sanatorium physicians realize that the treatment, as shown by Fales and Beaudet (6), must be prolonged and intensive.

SUMMARY

The prognosis in minimal tuberculosis is less benign than is suggested by sanatorium reports. Patients admitted to sanatoria several months after diagnosis or after onset of symptoms, and whose disease is still minimal in extent, as a rule have chronic lesions which respond well to treatment. Fresh lesions which may progress rapidly are frequently encountered among patients whose disease is detected in the asymptomatic phase by clinic or survey examinations. The seriousness of minimal tuberculosis is demonstrated by the occurrence of progression in more than a third of patients with minimal lesions observed at the Henry Phipps Institute.

REFERENCES

(1) Sampson, H. L.: Fatality rates in pulmonary tuberculosis, Am. Rev. Tuberc., 1939, *40*, 71.

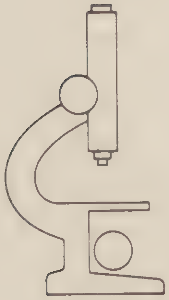
(2) Hetherington, H. W., Israel, H. L., and Kreitz, P. B.: The incidence and control of tuberculosis in high school children, Ibid., 1938, *38*, 406.

(3) Israel, H. L., and Payne, H. M.: Tuberculosis in the Negro, Ibid., 1940, *41*, 188.

(4) Hetherington, H. W., and Israel, H. L.: Tuberculosis in medical students and young physicians, Am. J. Hyg., Sect. A, 1940, *31*, 45.

(5) Israel, H. L., Hetherington, H. W., and Ord, J. G.: A study of tuberculosis among students of nursing, J. A. M. A., 1941, *117*, 839.

(6) Fales, L. H., and Beaudet, E. A.: The varying duration of the arrested stage, Am. Rev. Tuberc., 1937, *36*, 511.



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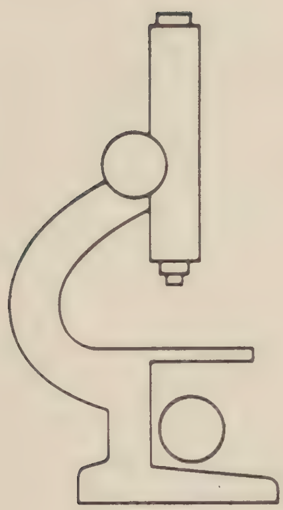

BRONCHIOGENIC CARCINOMAS

THE DIFFERENTIATION OF BRONCHIOGENIC CARCINOMAS*

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THE hopelessness with which cancer of any organ is regarded by the laity is reflected somewhat in the average physician's attitude toward bronchiogenic carcinoma. This attitude will continue to be one of hopelessness as long as cancer of the lung is considered a single disorder; as long as it is believed that a negative bronchoscopy rules out malignancy in from 75 to 85 per cent of cases; and as long as radiography is delayed until physical signs appear. An attitude of pessimism will prevail if it is believed that bronchiogenic carcinoma is clinically silent during the first half of its existence; if a policy of ''watchful waiting'' is regarded as a means of diagnosis, especially if during this period of observation the cancer extends beyond resectability. Too frequently precious time, the chief factor distinguishing curable from incurable cancer, is lost during the period in which a dry cough ''should clear up,'' or between the occurrence of hemoptysis and a careful investigation for its cause. Such delay may be an economic compromise or a consequence of inadequate diagnostic facilities, but occasionally it is adopted without thought of therapy because the disease is considered hopeless in the beginning.

Bronchial carcinoma, like cancer elsewhere, is a disease of later life; however, many of its victims are middle-aged, and others are good surgical risks despite their years. Naturally, it is disheartening to see an

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inoperable squamous-cell carcinoma in a 50-year-old man who has been "doctoring for half a year"; nevertheless, such occurrences should not provoke pessimism. On the basis of the excellent work of Koletsky,[1] the study of a series of cases, and my own observations, I believe that many bronchiogenic carcinomas are curable at the time of the onset of symptoms and that total pulmonectomy is a logical operation, a precise and truly surgical procedure. I should like to promote this conception to a wider acceptance.

My purpose, therefore, is first, to show that cancer of the lung cannot be regarded pathologically or clinically as a single entity; second, to indicate the diagnostic value of bronchoscopy in early cases; and finally, to show that time is really precious and that in many cases there is no significant silent period, but that symptoms tend to occur early. If they do occur early, and if too much significance is not attached to a negative bronchoscopy, and if we have a good fundamental knowledge of the clinical and pathologic behavior of bronchiogenic carcinoma, then perhaps we can fulfill Harvey's[2] ideal for the future, "Early diagnosis leading to radical treatment." Possibly in the future fullest use will be made of all available biologic, endoscopic, and radiologic methods of diagnosis;[3] and then, perhaps, we can supply better prognosis, perform fewer needless operations, reduce operative mortality, and increase the incidence of cures.

PATHOLOGICO-CLINICAL DIFFERENTIATION

This paper is based on the study of 216 patients admitted to Cleveland City Hospital whose cases were diagnosed primary carcinoma of the lung; 158 were histologically proved. In thirty-two the clinical diagnosis was regarded as correct; twenty-six were discarded as possibly misdiagnosed. Of the histologically proved cases, there were fifty-three small-cell carcinomas, thirty-two adenocarcinomas, and sixty-one squamous-cell carcinomas; five were diagnosed carcinoma simplex, and in seven there was insufficient material to make a diagnosis of tumor type (aspiration biopsies, pleural fluid).

Koletsky has reported the results of his study of 100 of the autopsied cases in this series. On the basis of histologic character, he recognized three essential types of bronchiogenic carcinoma: namely, small-cell carcinoma, adenocarcinoma, and squamous-cell carcinoma, which differed in the site of origin, rapidity of growth, and mode of extension and metastasis. The prominent distinctive features were those of type and not simply dependent on the degree of histologic differentiation. The latter did not seem to particularly influence the morbid anatomy of each type, nor cause one to resemble another; neither did it confuse the microscopic picture so that biopsy of the primary tumor was not indicative of type. As well as a correlation between cell type and gross morbid anatomy, Koletsky found a relationship between the latter and the clinical behavior and prognosis. The additional cases in this series

support these concepts. By careful clinical, bronchoscopic, and radiologic study it has been found possible to predict tumor cell type in the majority of cases before histologic examination.

Small-Cell Carcinoma.—Sixty-six per cent of these tumors arise in the main stem bronchi. The remainder frequently begin near the orifice of a secondary branch; rarely, the site of origin is in a small branch bronchus. The formation of an irregular mediastinal mass is characteristic of this centrally located and rapidly growing tumor. It is highly invasive, extends along the bronchus, and surrounds it and neighboring structures with firm tumor. This process is accompanied by a nonselective invasion of the adjacent lung. The involvement of pulmonary parenchyma, however, is less conspicuous than the mediastinal extens on which is vigorously metastatic to adjacent, regional, and distant lymph nodes (Fig. 1).

Fig. 1.—*A*, Surgical specimen. Right lung containing a local tumor mass, a rather early small-cell carcinoma. Death occurred on the twelfth postoperative day following sudden hemorrhage from the inferior pulmonary vein. The tumor arose in the orifice of the right lower lobe. Thirty-six autopsy sections of the mediastinum revealed microscopic tumor in one lymph node.

B, Autopsy specimen. Both lungs and heart. Huge mediastinal mass arising in the right main bronchus. Small-cell carcinoma with extensive mediastinal involvement, invasion of the heart, and occlusion of the superior vena cava and the bronchus. *T*, Tumor mass; *H*, heart; *L*, left lung. (See Fig. 8, *B* and *BB*.)

Early symptoms are cough and vague thoracic sensations. Hemoptysis may occur early but is more commonly a late symptom; it usually follows mucosal ulceration by tumorous invasion, or infection consequent to partial bronchial occlusion. As a rule, the former is only extensive at a late stage, and the latter tends to occur only after the tumor has grown to a good size. This follows the usual location of these tumors about large, rigid bronchi, deep in the mediastinum. Occasionally, but not commonly, the first symptoms which seem to warrant medical attention arise from metastases in the cervical lymph nodes or within the cranium, or from the involvement of mediastinal structures. Hoarseness may result from involvement of the vagus or recurrent laryngeal nerves; dyspnea and wheezing from bronchial occlusion or tracheal

compression; dysphagia from esophageal compression; and swelling of the upper body from vena cava compression. Such symptoms and findings may be the dominant features of the initial examination, but, as a rule, they were preceded by cough, chest pain, and even considerable weight loss.

It is a common belief that the properties which characterize a tumor as malignant are more pronounced when the tumor's victim is young. In a sense, this is true of the small-cell carcinoma which tends to occur in younger individuals (average age 47) than does adenocarcinoma or squamous-cell carcinoma. However, it does occur in the seventh decade, and in one instance a patient aged 35 survived for four years. It does not seem logical to infer that the small-cell type of tumor is only a highly malignant variety of a single disease, and not a distinct type of tumor.

Adenocarcinoma.—In this series the adenocarcinomas arose in secondary branches, such as the lobar stems, in 70 per cent of the cases; in small branch bronchi, in 20 per cent; and in the main bronchi, in 10 per cent. The central extension of this tumor is less striking than its peripheral growth which follows the bronchial and vascular channels. The rapidity of its growth varies somewhat with the degree of cellular differentiation but is less marked than that of the small-cell tumors. Because of its tendency to arise in secondary bronchi and small branch bronchi, it may form a well-circumscribed mass which replaces pulmonary parenchyma and which appears as a nodule within the lung. Such a location, in the richly vascular pulmonary tissue, is favorable for widespread and extensive blood-borne metastases, a common finding at autopsy. Lymphatic metastases are generous. There may be diffuse involvement of the mediastinal lymph nodes, with the formation of irregular masses. Involvement of the peripheral lymphatics may invoke pleural effusion, which may be bloody. In one instance there was fatal hemorrhage into the pleural space from a small peripheral tumor which had not metastasized.

On three occasions I have seen a peculiar gross behavior of adenocarcinoma which is rather striking. Because my experience is limited, I feel that this behavior may be rather common. In all three instances it was observed relatively early. One would expect full tumor growth to obscure this anatomic detail, so that it might not be detectable at autopsy. The tumor apparently arises deep in the bronchial structure, perhaps in a mucous duct or gland; it grows from there into the bronchus by perforating the wall between plaques of cartilage, thus forming a pedunculated, polypoid, intrabronchial mass (Fig. 2). Its growth external to the bronchus likewise is a circumscribed mass, and the entire tumor, therefore, is more or less bilobed, or like a ''cottage loaf'' as Brock[4] has so aptly put it. He, however, was referring to benign adenomatous polyps. In two of these three instances, the patients died with metastases (Fig. 3, *I* and *II*).

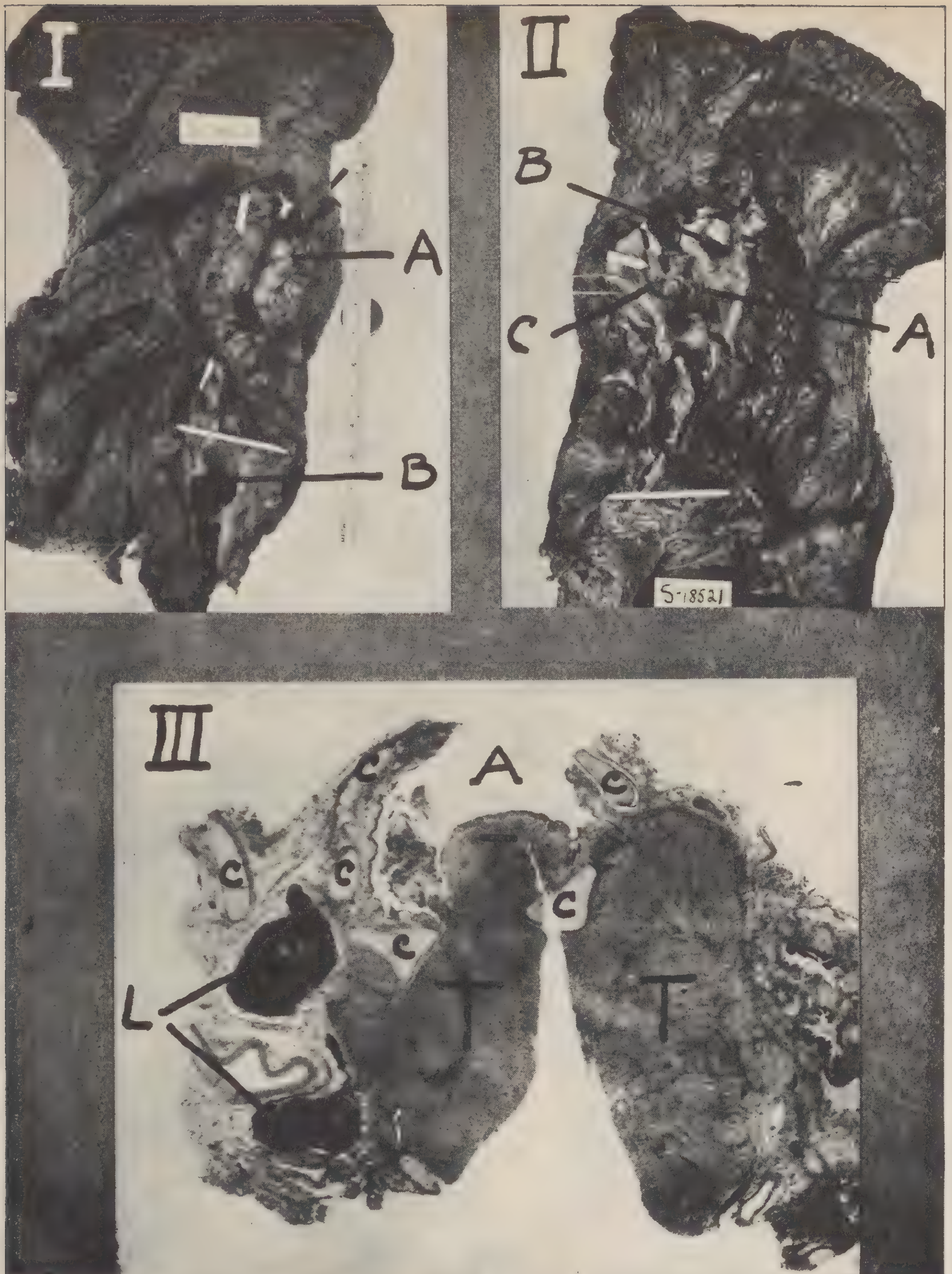


Fig. 2.—Surgical specimen of left lung, demonstrating a sharply circumscribed, well-differentiated adenocarcinoma of the main bronchus, with an acute tuberculous abscess in the lower lobe.

I, Posterior view of specimen with an incision in the tumor, *A*. *B* indicates the abscess in the lower lobe.

II, View of hilum. *A* indicates the bronchus which has been laid open; *B*, the upper lobe orifice; *C*, perforation of tumor and protrusion into the bronchus.

III, Photograph of a paraffin section of the entire tumor and the left main bronchus. The major portion of the tumor is without the bronchus and the minor portion enters the bronchial lumen between the cartilages. *A*, Bronchial lumen; *C*, bronchial cartilages; *T*, tumor; *L*, lymph nodes.

The short duration of the patient's illness and the rapid production of complete bronchial occlusion are the only facts which strongly favor the opinion that this tumor is not a benign adenoma. The fact that the patient is living and well more than two years following operation is not necessarily an argument against malignancy.

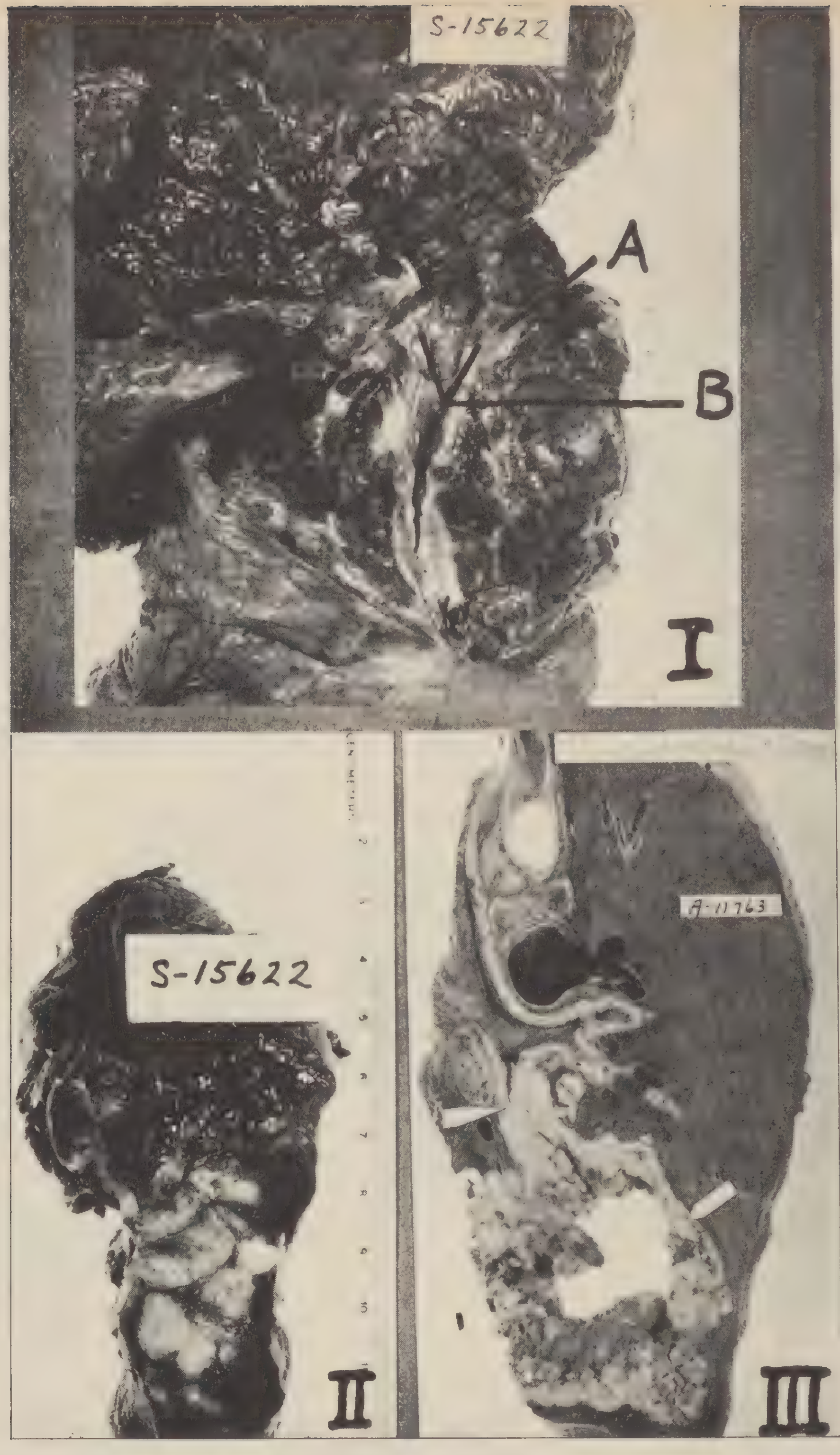


Fig. 3.—*I,* Surgical specimen of right lung, showing view of hilum. *A* points to the main bronchus which has been laid open and a portion removed. The defect reveals tumor just without the bronchus. *B* points to two crescentic defects in the bronchial wall where a polypoid tumor had protruded. At bronchoscopy it appeared to be a benign adenoma. Biopsy showed well-differentiated adenocarcinoma. The large mass of tumor, which existed outside the main bronchus, is shown in *II.* The patient died eighteen months after operation from recurrence of the tumor.

III, Autopsy specimen, showing left lung with a huge squamous-cell carcinoma exhibiting a large cavity. The tumor arose in the lower lobe bronchus. Note the peribronchial extension.

While benign adenomas have a predilection for women,[4] adenocarcinoma affects the same sex in 28 per cent of cases in striking contrast to 5 per cent in the small-cell and squamous-cell types. This mild similarity in sex affectation and in the occurrence of a detail in gross pathologic behavior may mean nothing, or it may be a feature of any early adenomatous tumor of the bronchus. It may also indicate, however, that a more profound relationship exists between benign bronchial adenomas and bronchiogenic adenocarcinoma.

Hemoptysis and pleural pain seem to be early symptoms more frequently in adenocarcinoma than in small-cell carcinoma. The pulmonary symptoms are occasionally absent or deemed insignificant, and the presenting complaint may arise from metastases. The average age in this group was 51 years, above that of the small-cell group. The average duration of life from the onset of notable symptoms to death was eight months.

Squamous-Cell Carcinoma.—In 70 per cent of instances this tumor originates in the first branches of the main stem bronchi. It apparently grows more slowly and affects older persons than either of the other two types, the average duration being twelve months, and the average age, 55 years. Local growth of the primary tumor results in the formation of a nodular mass about the bronchus of origin. In an early radiograph this may appear as a fairly well-circumscribed area of density, which has a tendency to central necrosis and cavitation. What role infection plays in this process cannot be stated when the cavitation occurs early. However, late in the disease, and especially at autopsy, it seems that infection plays a significant part. We know that it always does in long-standing bronchial obstruction. Such a state is common in the course of this slowly growing tumor, for it extends centrally along the bronchus, causing a fixation and constriction of this structure. This extension is not by way of lymphatics, and although it is invasive, it seems to avoid lymph nodes. It is extrabronchial in its proximal portion so that the lumen of the constricted bronchus may reveal mucosal tumor only deep within the entire mass. Peripheral growth of the mass is likewise invasive. Upper lobe tumors are prone to extend into the upper thoracic aperture, or into the chest wall, disturbing the function of adjacent structures. Such extension may be unaccompanied by notable metastases in the mediastinum. In general, this tumor seems to metastasize late and, even then, not nearly as extensively as small-cell carcinoma and adenocarcinoma. In contrast to these two types, the squamous-cell tumors exhibit cavity in over 50 per cent of autopsy cases. The cavity usually communicates with the involved bronchus and occupies the center of the peripheral tumor mass (Fig. 3, *III*).

The earliest symptom is usually cough which is productive. Pink or bloodstreaked sputum is quite common. The onset is rather in-

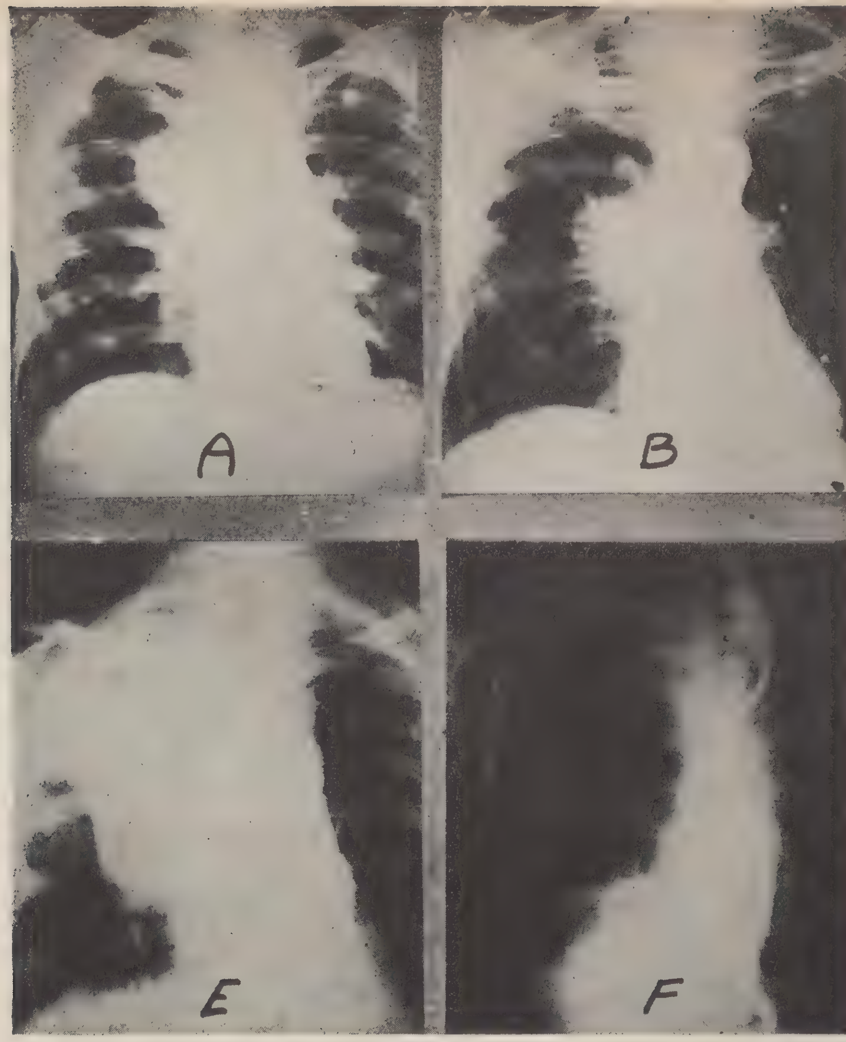
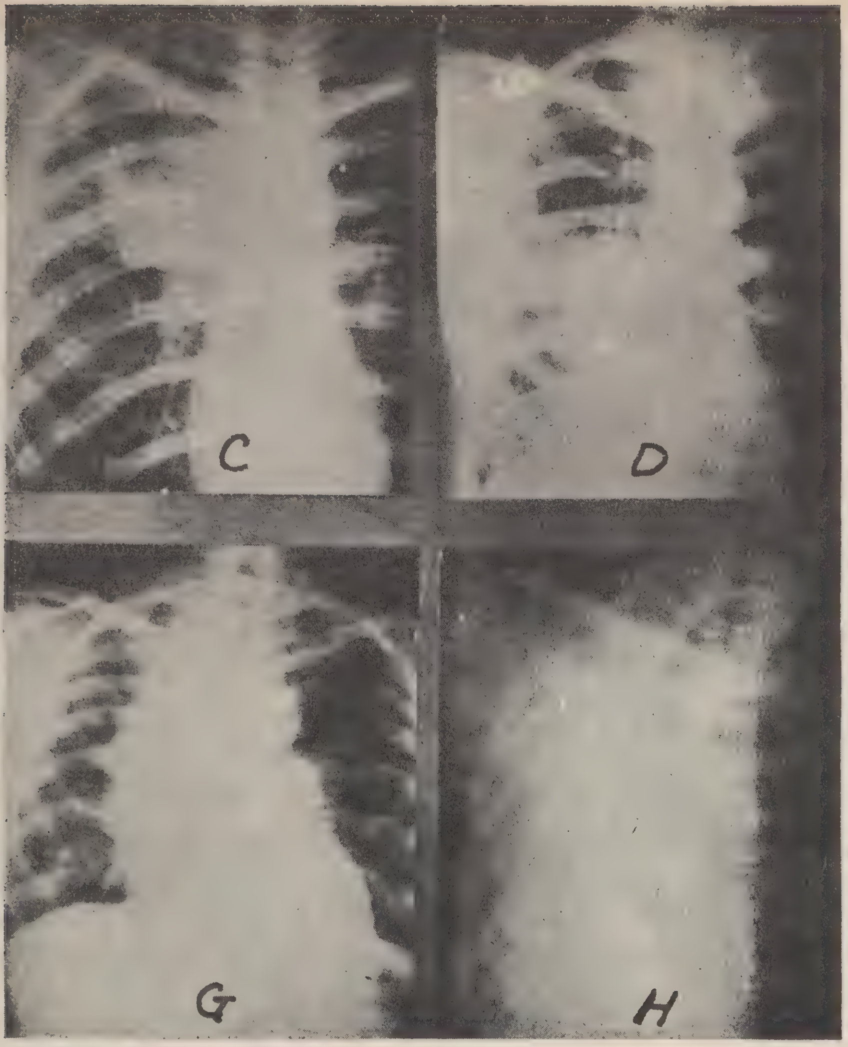


Fig. 4.—Eight examples of small-cell carcinoma. *A*, *B*, and *C* had symptoms for from one to two months. There is a rather poorly defined, dense, irregular mass blending with the mediastinum in each instance. *D* had symptoms for six months; the mass is large and there is considerable infiltration in the lower lobe. *E*, *F*, *G*, and *H* had

(*Continued on next page.*)

sidious, and the presenting illness may be of months' duration. Tumors high in the apex or near the parietal pleura are commonly accompanied by severe pain and may involve the brachial plexus or cervical sympathetic system. Later, infection with fever, productive cough, and weight loss are outstanding symptoms.

At the time that a maladjustment of natural phenomena occurs within a person, and as a result a few epithelial cells within the lung exchange their properties of function for increased growth and reproductive abilities and in such fashion become a bronchiogenic carcinoma, perhaps it would be difficult to separate one type of cancer from another. However, from this beginning, whether it is a common one or not, the subsequent courses are ordinarily divergent, and occur in three fundamental modes until the cancer destroys itself by killing its host. At



symptoms for from six to nine months. *E* shows beginning atelectasis; the patient had superior vena cava obstruction and hoarseness. *F* shows marked distortion of the esophagus. *G* shows a huge mediastinal mass without atelectasis. The patient had severe symptoms of mediastinal obstruction. *H* shows complete atelectasis of the right lung; usually a very late occurrence in small-cell carcinoma.

this time, at autopsy, we find the three essential types of bronchiogenic carcinoma as described by Koletsky. At this time, also, the distinguishing features which characterize each type are the most prominent. One wonders if such distinction can be made during life or early in the course of these tumors. This study indicates that it can be in the majority of patients; and, therefore, it is believed that each type has its own peculiarities at the onset, and that these differences become more pronounced as the disease advances. There are instances in which the characteristic features overlap, so that even the gross pathologic findings are not entirely conclusive and histologic study alone is differentiating. Naturally, there are even more such instances when only clinical data are available. Nevertheless, these instances are not the rule, and, in general, the gross morbid anatomy is reflected well enough in the clinical picture to enable one to separate the three essential types by such means as the combination of radiography and bronchoscopy.

Ordinarily each type of tumor produces a rather characteristic radiograph which, of course, is varied by the age and location of the tumor, the degree of bronchial obstruction and inflammation, and peculiarities of the host. Despite these variable factors, the gross morbid anatomy is distinctive enough to produce a radiograph which is frequently indicative of tumor type. Sometimes this is true relatively early in the disease, and later other factors, such as complete bronchial occlusion, hydrothorax, and infection, mask the true morbid anatomy and the radiograph is not distinctive.

Small-Cell Carcinoma (Fig. 4).—Early in the course of this tumor, about the time troublesome symptoms begin, it is not unusual to see an irregular mass in the radiograph which blends with the mediastinum and does not have a sharp outline. Surrounding infiltration, which is mostly inflammatory, is usually scanty, but may be rather extensive and clear spontaneously. Lobar atelectasis is not common except when the primary tumor arises in a secondary bronchus. The primary mass enlarges rapidly and extends principally into the mediastinum, thereby producing distortion of the mediastinal structures but usually not much atelectasis. Finally, there is severe ''choking'' of the mediastinum which may or may not be accompanied by main bronchial occlusion.

Adenocarcinoma (Fig. 5).—The early radiograph frequently displays a sharply circumscribed, dense mass which, for the most part, is separate from the mediastinum. There is usually no evidence of mediastinal involvement. Infrequently a mass, which may be a small tumor and still the source of widespread metastases, is hidden by the mediastinal shadow. However, if the primary tumor is not visible and has not produced some atelectasis, in all probability it is an operable, local tumor. Late in the disease there is little to distinguish adenocarcinoma from the other types besides the fact that it is more prone to produce secondary tumor nodules in both lungs. There may be a large mass of mediastinal tumor simulating small-cell carcinoma; and rarely the primary tumor cavitates, thus simulating the squamous-cell type.

Squamous-Cell Carcinoma (Fig. 6).—The early radiograph portrays a nodule in the lung which is not entirely peripheral and less sharply circumscribed than the primary adenocarcinoma. The original tumor may be indistinct because of surrounding inflammatory infiltration, a rather common accompaniment. Growth of the tumor tends to produce occlusion of a secondary bronchus (where it originates in 70 per cent of cases) and to cause a simple lobar atelectasis. Necrosis and cavitation of the primary tumor may occur early and make the radiograph indistinguishable from that of lung abscess. In the course of time the tumor extends along the bronchus into the mediastinum and peripherally into the lung. It may thus produce multilobar atelectasis,

form a giant cavity, extend into the chest wall, or into the thoracic inlet, and interfere with contiguous structures.

The inference that the radiograph is a super-microphotograph that labels bronchiogenic carcinoma one type or another is not intended, but it is hoped that the accompanying figures and statements portray the relationship existing between the gross morbid changes of each tumor type and the clinical picture they produce. In many instances, late in the disease, it is possible to obtain an "inside" view of the morbid anatomy by bronchoscopy, and such observations combined with clinical and radiologic studies often provide a complete picture.

BRONCHOSCOPIC DIFFERENTIATION

Small-Cell Carcinoma (Fig. 7, *I*).—Because of a frequent origin in the main bronchus and because of a tendency to form a large mediastinal mass, the majority of small-cell tumors present typical bronchoscopic findings of which the most common are extreme distortion and fixation. When bronchoscopy is performed late in the disease, the tracheobronchial tree is firmly fixed. The lower trachea may be compressed; enlarged lymph nodes deforming the soft posterior tracheal wall may be palpated with the lip of the instrument. The growth of tumor at the bifurcation tends to pry the main bronchi apart. If this takes place rapidly and is observed shortly after its occurrence, the mucosal edge of the carina may still be sharp, although the angle of bifurcation is much widened. This finding is not unusual in recent inflammatory enlargement of the bifurcation lymph nodes. Later on, the carina becomes a rounded surface rather than a sharp edge. The mediastinal mass may compress the bronchial lumen into a narrow slit, so that it is impossible to see distally where the tumor has broken through the mucosa. At other times the involved bronchus may be an irregular, tubular structure of tumor, which is not occlusive and provides ample areas for biopsy.

Adenocarcinoma (Fig. 7, *II*).—Bronchoscopy may be entirely negative despite a good-sized tumor within the pulmonary parenchyma. On the other hand, the findings may be suggestive of an entirely endobronchial tumor. How this tumor perforated the bronchus in three cases has been mentioned above; it has not been observed in any other malignant tumor. Late in the disease there may be extensive mediastinal involvement, with deformity of the central portion of the tracheobronchial tree such as one sees in small-cell carcinoma. However, the fixation is somewhat less because the tumor occurs in partially separate masses, at the sites of lymph node concentrations, rather than in a single large tumor.

Squamous-Cell Carcinoma (Fig. 7, *III*).—On rare occasions, when this tumor originates in the main bronchus and bronchoscopy is performed very late, the findings may simulate those observed in small-cell tumors. As a rule, they are quite different. When the upper lobe

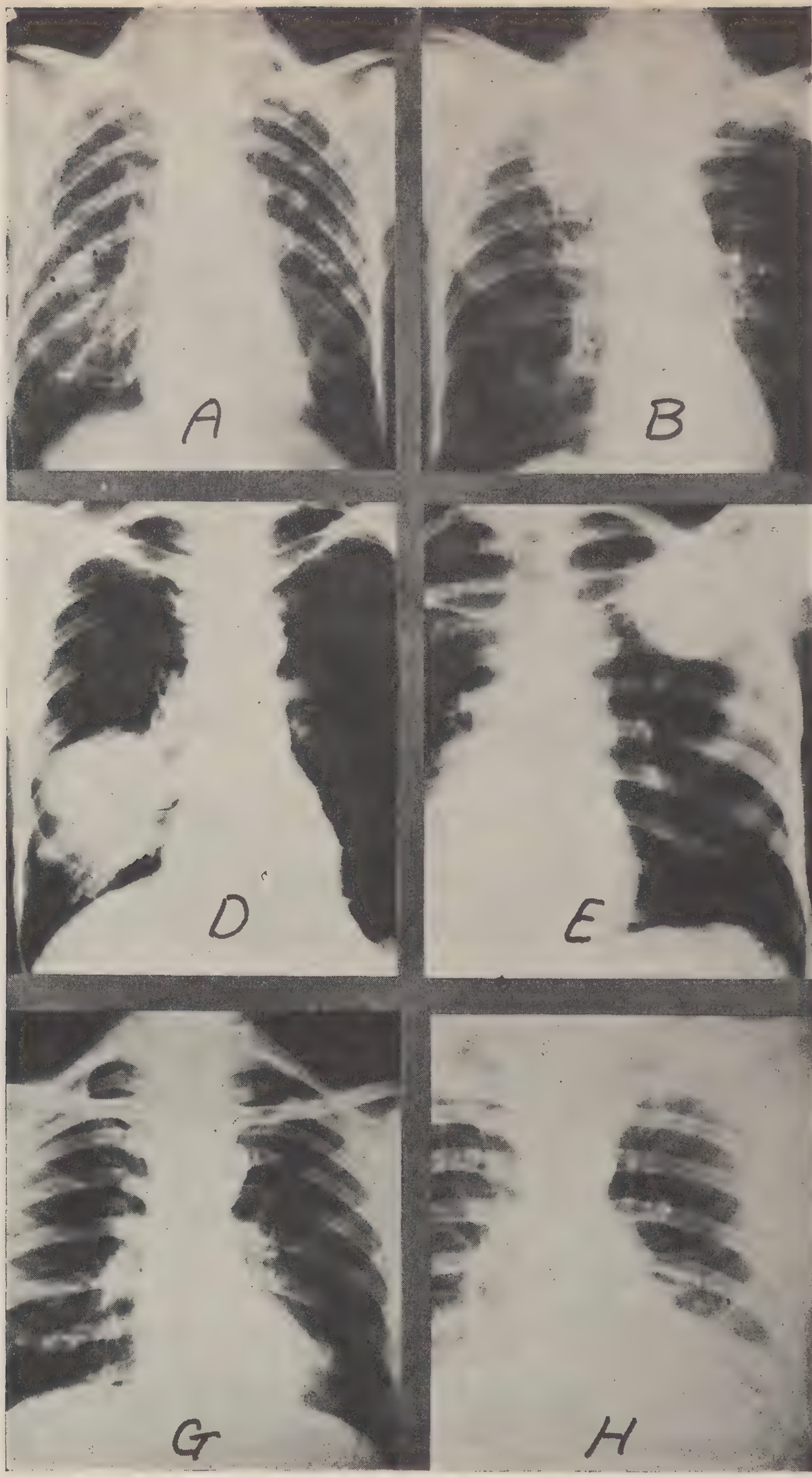

A
B
D
E
G
H

Fig. 5.—Nine cases of adenocarcinoma. *A, B, C, D* and *E* had symptoms for from one to six months. Each presents a sharply circumscribed, fairly regular, dense mass which is more or less separate from the hilum. *F* had symptoms for eight months. *G, H,* and *I* had tumors hidden by the mediastinal shadow. In *G* it was found in the left lower lobe bronchus by bronchography; in *H,* in the left main bronchus at bronchoscopy; in *I,* in the right upper lobe bronchus at autopsy. This radiograph was interpreted to indicate congestive heart failure. Tumor cells were present in bilateral pleural effusions. There were widespread metastases. Autopsy was performed three weeks after this radiograph. Complete removal of the tumor was accomplished in *D.* The patient died from pulmonary edema following thoracoplasty which was done three weeks after pulmonectomy. Autopsy revealed no tumor. *H* is an early radiograph of the case in Fig. 2.

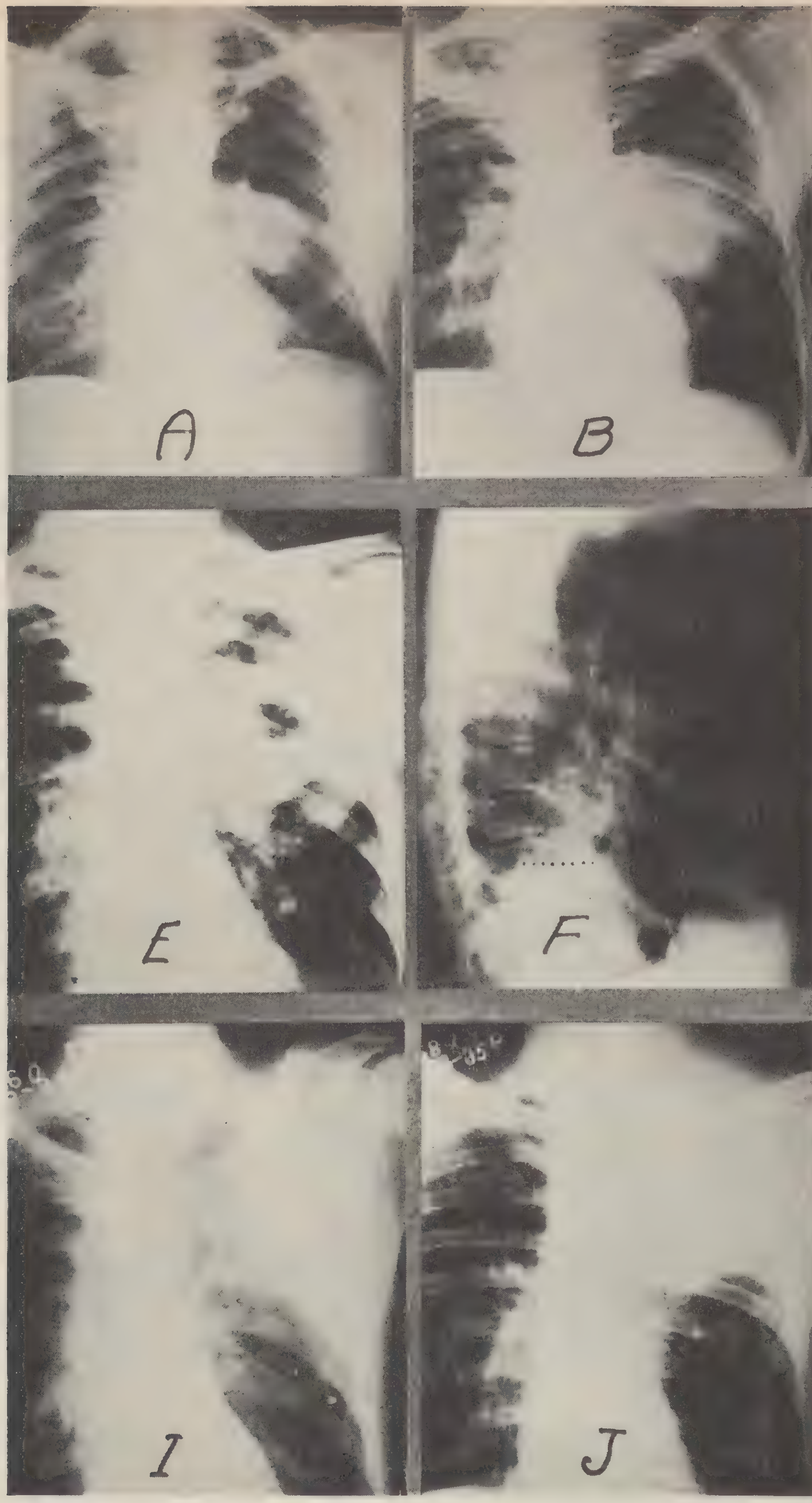
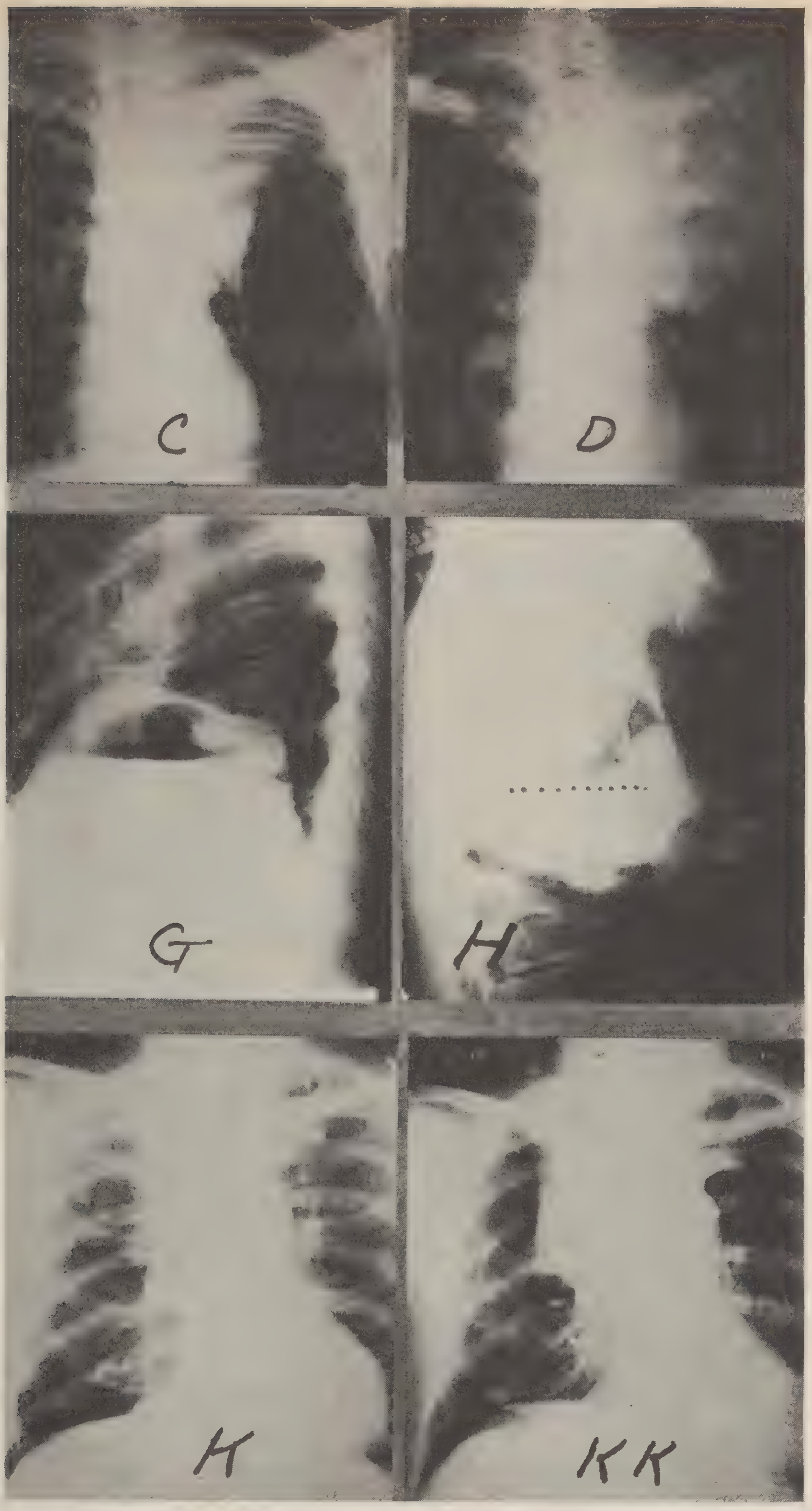


Fig. 6.—Eleven cases of squamous-cell carcinoma. *A* and *B* had symptoms for two months. The shadows are not as sharp or as dense as those seen in the adenocarcinomas. They do not blend with the mediastinal shadow as in early small-cell or main bronchus tumors. *C* shows a typical lobar atelectasis. *D* portrays a drowned upper lobe simulating pneumonic consolidation. In *E* and *F* there is cavitation of the



primary tumor mass, simulating lung abscess. *G* and *H* demonstrate giant cavities probably resulting from the necrosis of tumor which has almost completely replaced an entire lobe. *I* shows involvement of the chest wall, a behavior which seems uncommon in other than squamous-cell tumors. *J* and *K* had extension into the upper thoracic aperture, a behavior which is not unusual in squamous-cell tumors arising in the upper lobe bronchi. *KK* was made after the institution of pneumothorax.

bronchus is involved, bronchoscopy may be negative; however, if the bronchus is occluded, there is a telltale mediastinal shift and a slight climb of the hilum which increases the normal curvature of the main stem with the upper lobe bronchus; thus, it may be impossible to see its orifice. Occasionally a retrograde telescope will permit visualization

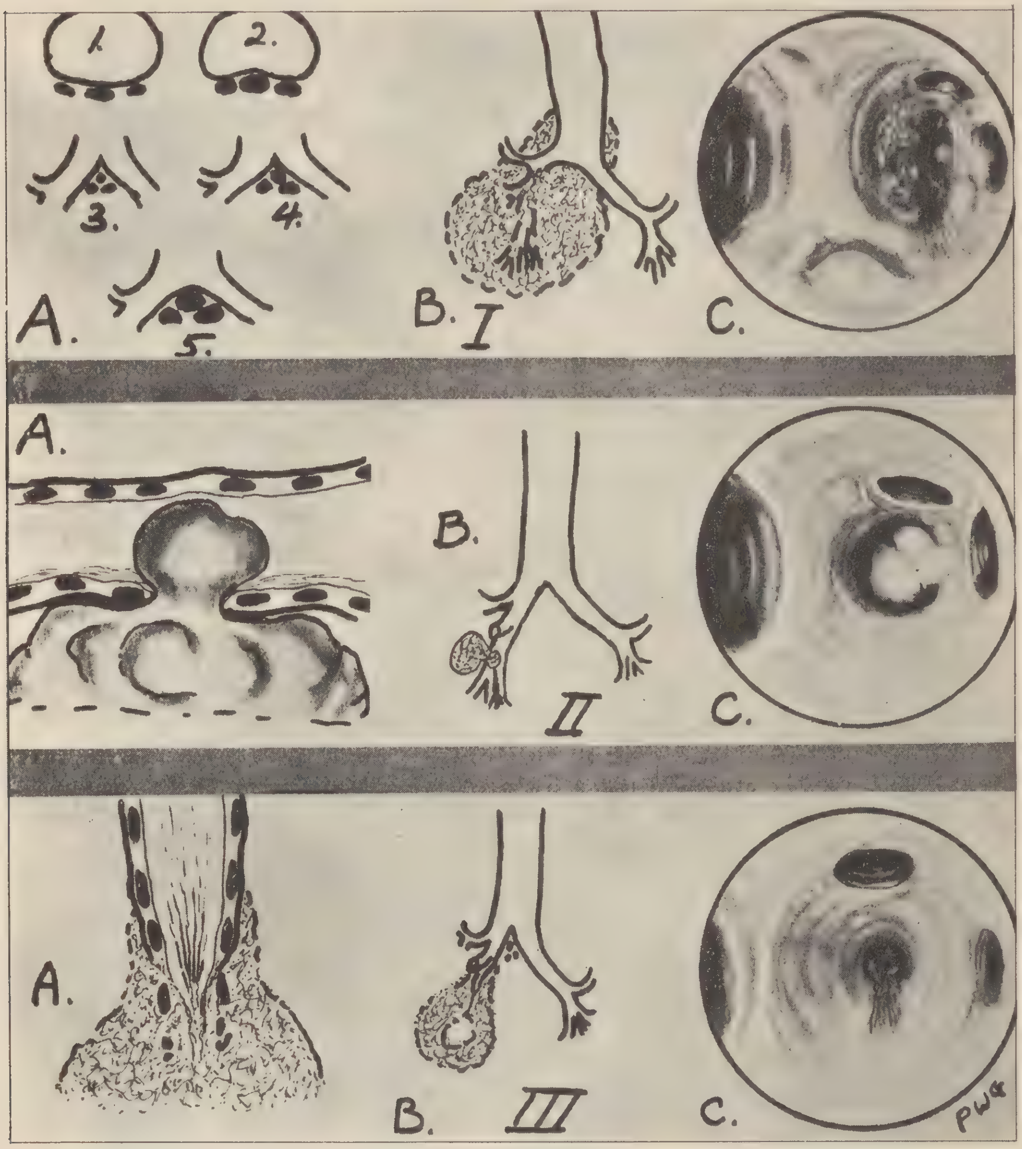


Fig. 7.—*I*, Small-cell carcinoma. *A* shows effect of enlarging lymph nodes on the tracheal cross section, and on the carina and bifurcation. *B*, Diagrammatic representation of a small-cell mediastinal mass arising in the right main bronchus. *C*, Drawing of a rather common picture at bronchoscopy. The angle of bifurcation is widened and the carina rounded. The posterior tracheal wall is irregular because of enlarged lymph nodes. Although the main bronchus is compressed, it is still patent.

II, Adenocarcinoma. *A*, Diagnostic sketch of bronchial perforation by adenomatous tumor. *B* and *C* indicate how such a tumor may appear to be entirely endobronchial. This has been observed three times in a rather small series. No other bronchoscopic finding has been noted as characteristic of adenocarcinoma alone. (See Figs. 2 and 3.)

III, Squamous-cell carcinoma. *A*, Sketch demonstrating how extrabronchial tumor may compress the bronchus and accentuate the longitudinal mucosal folds. This has been a frequent observation in squamous-cell tumors. *B*, Diagrammatic representation of a cavitating squamous-cell tumor arising in the right lower lobe bronchus. *C* indicates how it may appear through the bronchoscope. Normal bifurcation; main stem bronchus fixed; contracted lower lobe bronchus with deep longitudinal mucosa folds above the visible tumor.

of a deformed bronchus, but a biopsy must be taken blindly. At other times, a diagnosis can be made, without visualization of the tumor, from the displacement and contraction of the upper lobe orifice and the degree of bronchial fixation. Tumors arising in the other lobar bronchi are usually visible. There may be no deformity of the carina and bifurcation even late in the disease.

This tumor extends peribronchially. It tends to spare lymph nodes and the bronchial mucosa at its advancing edge. We usually see an ulcerostenotic lesion, at the site of origin deep in the bronchus, with a conical constriction above it. This latter deformity is one of contraction produced by the extramucosal infiltration of tumor. It fixes the bronchus in a contracted state, greatly accentuating the normal longitudinal mucosal folds. Later the tumor extends into the mucosa, and with the aid of infection produces a contracted, angry red bronchus almost replaced by tumor. This change may extend to within 1 or 2 cm. of the carina without the production of notable deformity of the bifurcation. Such peribronchial extension may invade a large vessel and cause death by hemorrhage; in the lower lobe bronchi it may surround and involve the inferior pulmonary vein in the apex of the pulmonary ligament and make surgical removal impossible. In left upper bronchial tumors, it may involve the recurrent laryngeal nerve long before tumor gains the lumen of the main bronchus.

It must be remembered that the radiologic and bronchoscopic differences as depicted above are merely reflections of gross morbid anatomy, and that in some instances the latter is not entirely differentiating. These instances, however, are exceptions to the rule. An attempt was made, after shuffling the cases in this series, to guess the type of tumor from a study of the clinical record obtained on admission, the admission chest roentgenogram, and the bronchoscopic findings. A correct guess was made in 90 per cent of the squamous-cell tumors, in 55 per cent of the small-cell tumors, and in 20 per cent of the adenocarcinomas, so that in the entire group it was possible to name correctly before biopsy the type of tumor in over 60 per cent of cases.

THE DIAGNOSTIC VALUE OF EARLY BRONCHOSCOPY

In this series a positive biopsy was obtained in 72 per cent of more than 100 bronchoscopies, and a diagnosis of carcinoma was made in 87 per cent of patients. At times, although there is little doubt in the diagnosis, it is impossible to obtain tissue for examination. These figures are similar to those found in the current literature and are in keeping with the observation that about 25 per cent of autopsy cases fail to reveal tumor which would be accessible for biopsy. The literature abounds with the statement that a positive biopsy can be obtained by bronchoscopy in 75 to 85 per cent of patients with bronchiogenic carcinoma. Such statements are misleading, for they are based on a rationale which has no regard for time and are frequently interpreted

to mean that a negative bronchoscopy rules out cancer in 75 per cent of cases. A tumor may be a small, peripheral nodule when it first causes hemoptysis and a large mediastinal mass when it is first observed bronchoscopically; so it is most important to consider the time of examination in relation to the onset of symptoms. It has been said, "By the time they're bronchoscoped they're too far gone to carry their own x-rays." In this series much of the clinical material is practically autopsy material, for the average duration of life from admission to death is only one month. Figures based on findings at this stage of the disease cannot be applied to patients examined at the onset of symptoms, which is the time a diagnosis should be made if there is ever to be any significant therapeusis for bronchiogenic carcinoma.

Assuming that symptoms generally occur early, we can estimate the value of early bronchoscopy by studying the tumor incidence in that portion of the bronchial tree within range of the bronscope. In this series 35 per cent of the tumors arose in the main bronchi, 26 per cent in the upper lobe bronchi, 26 per cent in the lower lobe bronchi, and 13 per cent in the middle lobe bronchus or in small branch bronchi. Very few of the upper lobe tumors, none of the branch bronchus tumors, and not all the lower lobe tumors would be visible early in their course. In all probability, if performed early, bronchoscopy will be negative in roughly 40 per cent of cases. If we consider squamous-cell carcinoma separately (the most common type of tumor and the most favorable for excision), we find that 49 per cent originate in the upper lobe or small branch bronchi. These are not likely to be accessible for biopsy until rather late in the disease. It seems logical to conclude that, in a patient with a short history in whom there is reason to suspect bronchial malignancy, a negative bronchoscopy means only that bronchography, sputum examination for tumor cells, aspiration biopsy, or thoracoscopy should be performed until there is sufficient evidence to warrant exploration or a diagnosis is established. For if tumor is being dealt with, it is probably operable and one should not "wait to see what happens."

DURATION AND ONSET OF SYMPTOMS

The average period between the beginning of a bronchiogenic carcinoma and the time at which it causes death is variously estimated between one and two and one-half years. Two years is the most common estimate. Naturally, such a figure is more of a guess than an estimate, for there is no real way of knowing how long a tumor has existed when it first causes symptoms or when it is first discovered. Usually such estimates are based on cases which happened to be observed early and ran prolonged courses. Uncontrolled clinical observation even over long periods tends to exaggerate the importance of these cases. The impression induced by their prolonged stay on the ward is deeper than that made by the moribund patient who is hospitalized and dies the

next day. There are numerous instances of both types in this series, and the average duration of life from the onset of notable symptoms was from six months to one year, depending on the type of tumor. There are so many factors which influence this duration, such as the age and condition of the patient, the location of the tumor, the type and severity of the accompanying infection, the location of metastases and so on, as well as the actual rate of growth and the invasive powers of the tumor, that it is difficult to evaluate its significance. The same multiplicity of factors acts in the production of symptoms. A peripheral tumor may not cause symptoms until it metastasizes, causes a pleural effusion, or grows to a large size. On the other hand, it may cause hemoptysis or chest pain early in its course, while only a small nodule. After all, we are not interested in how long the patient lives after he becomes sick except to provide ourselves with data for prognosis, but we are interested in knowing how extensive the average tumor is when it produces symptoms. For if they occur early, there is every reason to believe that surgical excision will be curative.

Jackson[5] has stated: ''In a few instances the biopsy has been done so early that there has been no recurrence of the growth; it was adequately removed at the diagnostic bronchoscopy.'' Certainly these patients must have had symptoms warranting bronchoscopy and just as certainly these must have been early symptoms. In this series there are a number of cases with durations exceeding two years, all of which had symptoms from the beginning, and there are others in whom small, isolated tumors were disclosed although there had existed a considerable period of symptomatology (Fig. 8). Mason has stated: ''But it is unfortunately probable that quite a number of cases seek medical advice, and are even admitted to the hospital in an operable state, but owing, perhaps, to procrastination or to doubt as to the efficacy of surgery, they reach the surgeon either too late, or not at all.'' (Fig. 8, *F* and *FF*.)

In cases such as those presented in Fig. 8, it is possible that cures might have been accomplished if surgery had been performed at the time of the first radiograph; and it is highly probable that surgery would have been curative had it been performed shortly after the onset of symptoms. The cause for such errors lies in too light a regard for time and the failure to apply rapidly all the available diagnostic measures, including surgical exploration.

Somewhat from this study, but more so from personal observations, I have come to the conclusion that symptoms tend to occur early in bronchiogenic carcinoma, and that those patients who have no pulmonary complaints until the tumor is hopelessly advanced or who feel well until metastases occur are exceptions to the rule. Physical examination, bronchoscopy, and even the posteroanterior radiograph may be negative at the onset of symptoms, but special radiographic studies

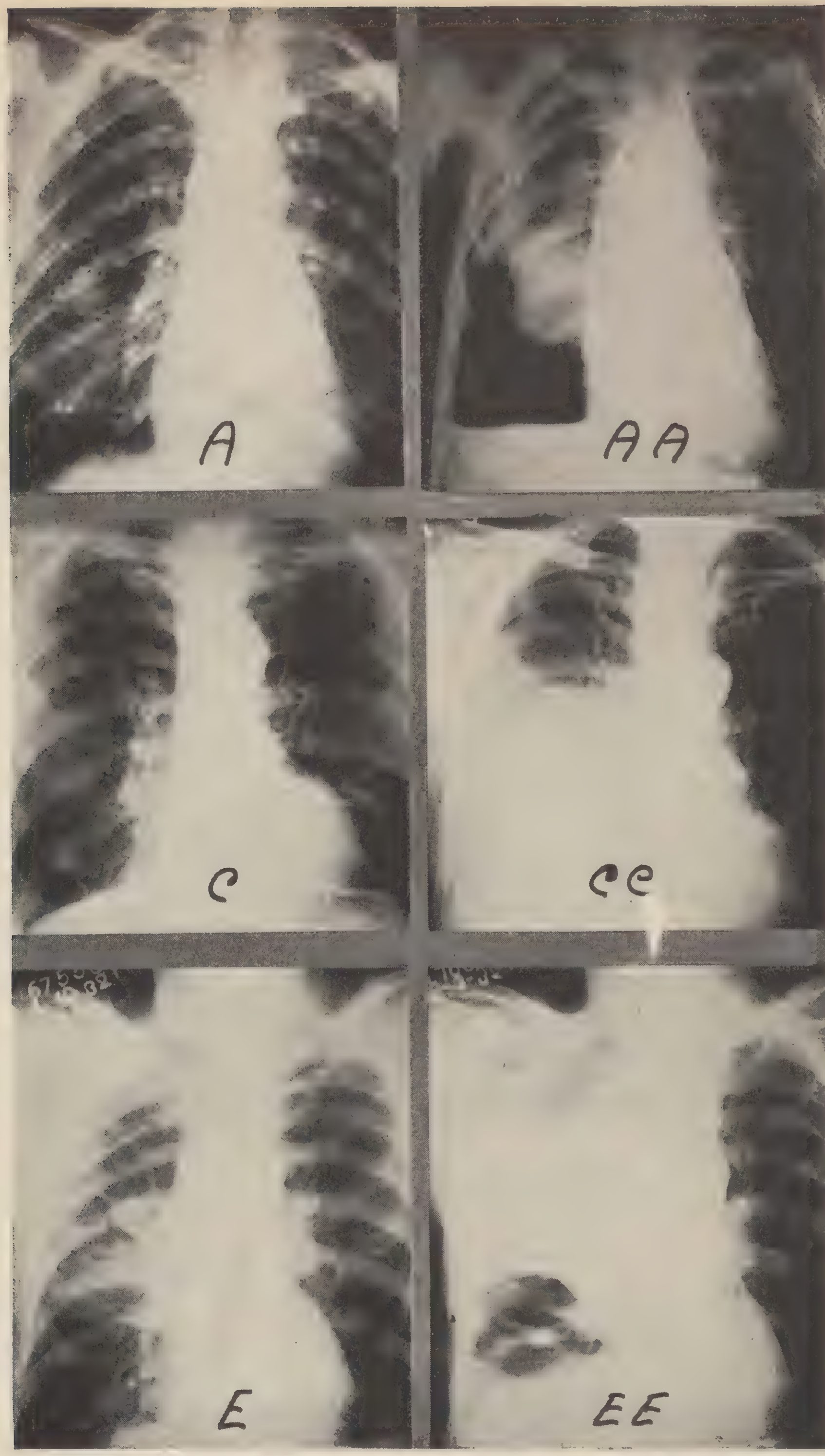
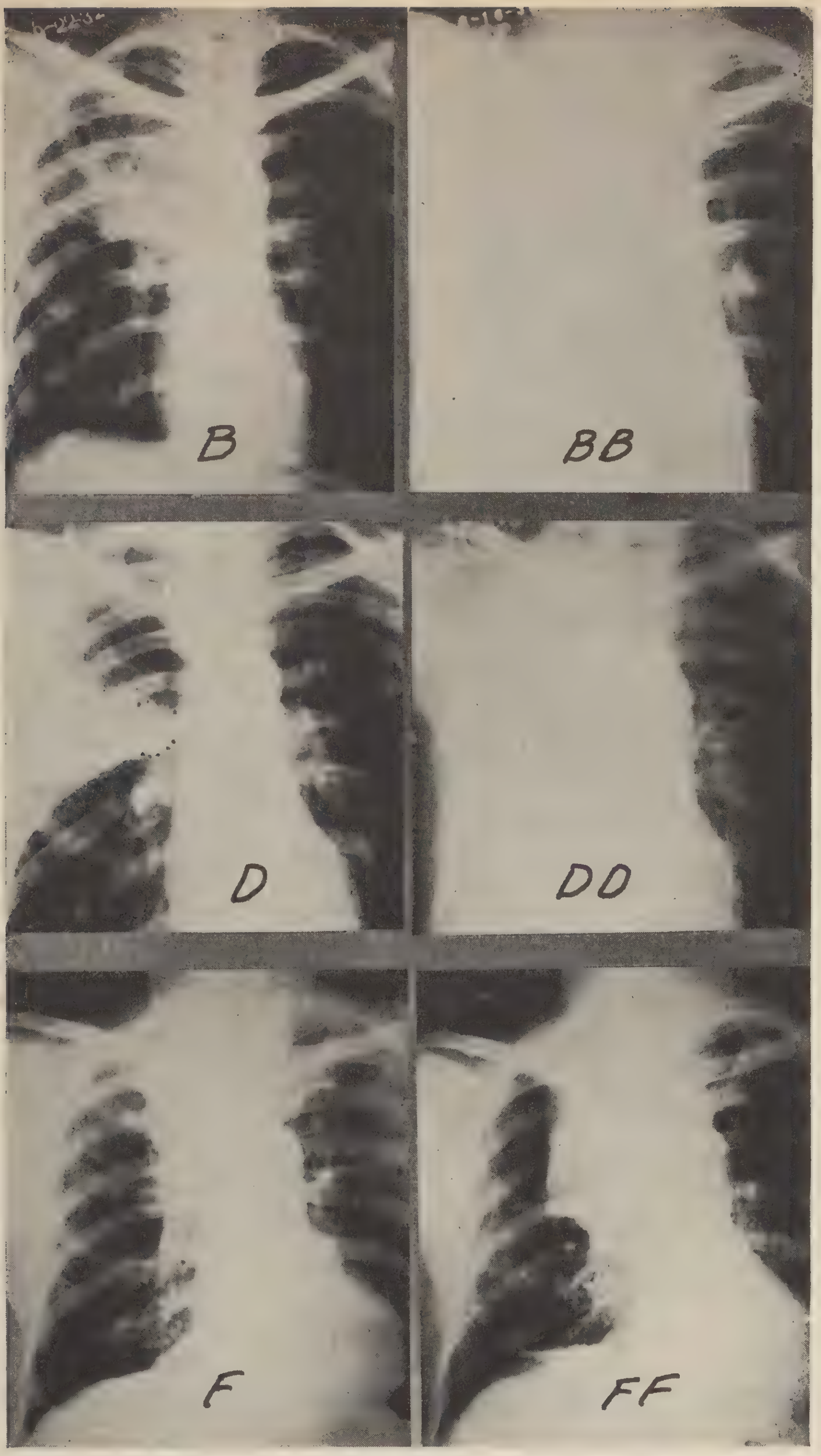


Fig. 8.—Examples of early symptomatology. *A*, This patient had visited the dispensary and complained of cough and chest pain for one month. Radiograph *A* was taken, and no follow-up was made until admission three years and four months later (*AA*). During this time pain, cough, hemoptysis, and weight loss had been progressive. *AA* was taken after aspiration of fluid and institution of air. Death occurred five months after admission. Autopsy showed adenocarcinoma.

B, The patient had had all the usual symptoms of bronchial carcinoma for two months (*B*); four years later, *BB*. Autopsy showed small-cell carcinoma (Fig. 1*B*).

C, Cough and chest pain had been present for eight months when this radiograph was taken. There is a small, irregular mass in the lower right hilus. *CC* was taken almost one year later. Autopsy revealed small-cell carcinoma of the right main bronchus.



D, The patient had had typical symptoms of bronchiogenic carcinoma for seven months. Radiograph shows a faint but regular mass adjacent to the mediastinum. The fan-shaped shadow represents atelectasis in the apex of the lower lobe. *DD* was made five months later. Autopsy showed adenocarcinoma of the right lower lobe.

E, Radiograph, taken seven months after onset of symptoms, shows an irregular, enlarged hilar shadow and a small dense mass bearing a cavity. *EE* was taken six months later (pneumothorax present). Autopsy revealed squamous-cell carcinoma arising in the right upper lobe bronchus.

F, Radiograph taken ten weeks after the onset of chest pain and cough. The patient consulted a physician two weeks after onset. Exploration was not performed until three months after *F* was made. *FF* was taken with pneumothorax just preceding exploration. An inoperable squamous tumor arising in the right upper lobe was found.[3]

and careful bronchography as well as other methods will reveal the cause for complaint. Total pulmonectomy is the way to remove it.

SURGICAL DIFFERENTIATION

The separation of the three essential types of bronchiogenic carcinoma as outlined above has led to certain conclusions in regard to surgical treatment which, in brief, are as follows:

Small-Cell Carcinoma.—Because of its central location, rapid growth, and potent invasive and metastatic powers, there is little hope that many cases will ever be cured by excision. However, those tumors arising in secondary bronchi which are diagnosed early may be completely removed by pulmonectomy. The presence of a large mediastinal mass, esophageal deformity, and vocal cord or diaphragmatic paralysis are considered contraindications to exploration. The same is true of certain bronchoscopic findings, such as: tumor within 2 cm. of the carina; enlarged, hard paratracheal lymph nodes; and widening of the bifurcation, with fixation of the carina.

Adenocarcinoma.—Those tumors arising in the periphery of the lung are most favorable for excision, but are inaccessible for tissue examination. In peripheral tumors aspiration biopsy under fluoroscopic control may frequently provide a histologic diagnosis. However, it is not a harmless procedure; the chances of disseminating the tumor or producing air embolus are good. It should not be attempted in early tumors within the hilus or if the possibility of lung abscess exists. The delay incurred by repeated attempts to obtain a biopsy by simple methods is probably more harmful than exploratory thoracotomy. Distant metastases, secondary nodules in the lung, pleural fluid containing tumor cells, and bronchoscopic evidence of mediastinal invasion contraindicate surgery.

Squamous-Cell Carcinoma.—This type of tumor is undoubtedly the best suited for surgical removal. Its frequent origin in secondary bronchi, relatively slow growth, and mild metastatic tendencies favor the possibility of complete removal. Those tumors arising in the lower lobe bronchi are within reach of the bronchoscope early, and are so located that wide resection is feasible. After they have extended up to within 2 cm. of the carina, in all probability mediastinal invasion is present despite the fact that there may be no indication of its existence. Invasion is most apt to occur in the apex of the pulmonary ligament about the inferior pulmonary vein. In like manner, the upper lobe tumors invade the hilum, encasing the pulmonary artery with tumor and frequently involving the mediastinal pleura. Although such extensions occur late in both lower and upper lobe tumors, histological diagnosis in the latter is difficult before the tumor extends into the main bronchus; only exploration will yield material for biopsy. Such exploration should not be delayed. Horner's syndrome, brachial plexus

disturbances, vocal cord or diaphragmatic paralysis, extensive rib destruction, and extreme bronchial fixation are considered contraindications to exploration.

Although some of the above conditions might not always prevent removal of the entire gross tumor, it is felt that in such instances the chances of adequate resection are too remote and that pulmonectomy should be reserved for those patients in whom there is reasonable hope for cure and in whom the removal of one lung will not result in useless, hopeless invalidism.

CONCLUSIONS

Pathologically and clinically, small-cell carcinoma, adenocarcinoma, and squamous-cell carcinoma are three fundamental types of bronchiogenic cancer.

The differences of these types early in the course of the disease sometimes permit their distinction by combined clinical, radiologic, and bronchoscopic investigations. Late in the disease this is true in approximately 60 per cent of cases.

Bronchoscopy will be negative in 40 to 50 per cent of cases if performed at the onset of symptoms. When negative, it should be supplemented by other biologic, endoscopic, and radiographic diagnostic methods until the cause for symptoms is known.

The impression that clinical symptoms tend to occur early, when the tumor is in an operable state, has been gained from this study. Therefore, it is felt that if diagnosis is made early and there is the proper selection of operative material, surgical treatment will gain a respectable position in therapeusis.

REFERENCES

1. Koletsky, S.: Primary Carcinoma of the Lung, Arch. Int. Med. **62**: 636, 1938.
2. Harvey, C.: Cancer of the Lung, M. J. Australia **1**: 565, 1936.
3. Mason, G.: The Clinical and Surgical Aspects of Thoracic Neoplasms, Proc. Roy. Soc. Med. **32**: 1346, 1939.
4. Brock, R.: Pulmonary New Growths, Lancet **2**: 1041, 1938.
5. Jackson, C.: Malignant Growths of the Lung, Arch. Otolaryng. **12**: 747, 1930.

DISCUSSION

DR. W. E. BURNETT, Philadelphia.—This excellent paper was most interesting and convincing. I had the opportunity of seeing it before this meeting, when Dr. Gebauer sent it in for examination. I am very pleased to hear that it was awarded the prize for excellence. I think this award is justly deserved, and I am sure you who have just heard the paper will all agree. It was so logical and convincing that it made one fear the obvious and resort to his own files to see how closely he could check up.

I have a few examples of cases drawn from that group. I might say at this time that in the last five years we have had 102 cases under observation in the Temple University Hospital, most of which were referred from the Jackson Clinic. Of these, we have been able to explore in about thirty-four patients in whom we found no evidence of distant metastasis. Of the thirty-four, pneumonectomy for carcinoma has been done on twelve cases.

Some of these cases are the ones I should like to present now to indicate our attempts to apply Dr. Gebauer's classification, realizing, of course, that we were not well instructed in his thought and had very little time in which to study the paper and slides to acquaint ourselves thoroughly with his standards.

(Slide) This first case, as classified by Dr. Gebauer's criteria, would be called a squamous-cell, and proved to be so on biopsy.

(Slide) This was the specimen removed at operation, showing the location of the tumor extremely high, so high that bronchoscopically it was questionable whether this tumor was removable. Having removed it at the location you see there, we realized we were very close to the tumor so we took off an additional, in fact, the last, centimeter of bronchus, and trimmed the trachea down, tapering it to the other side and obtaining a good closure by Rienhoff's method. The pathologists found no tumor in the additional bronchial segment. This man made an uneventful recovery.

(Slide) This shows the bronchus open to reveal the high location of this tumor and its type of contracture.

(Slide) This is postoperative by four months, and the subsequent one nine months later.

Here is the film of a patient about whom there was some question in my mind. I felt this might be interpreted by Dr. Gebauer's standards as adenocarcinoma, but there is a suggestion of cavitation in it. I showed it to Dr. Gebauer a little while ago and he said, "Yes, that is squamous." And so it was microscopically.

(Slide) This man also had a pneumonectomy, and this is a specimen showing the tumor in the lingula of the upper lobe, as a fairly well-circumscribed affair. (Slide) It surrounded the whole bronchus and contracted it down to complete closure. This is the mediastinal side of that same lung, which showed no glandular involvement. This man also made a good postoperative recovery.

(Slide) The next to the last patient for demonstration was one of the earliest cases we had. This small tumor is a little difficult to find, but can be seen to the left of the cardiac shadow, and on the lateral film in here. This was reached by needle biopsy, because bronchoscopy could not visualize it. This brings to mind the fact that routinely all methods are utilized and bronchoscopic negatives do not mean that we give up the search, of course.

(Slide) This lung was removed and corresponds entirely to the x-ray view. This was a small-cell carcinoma, as Dr. Gebauer called it when I checked him up a few minutes ago.

This is a patient with blockade of the lower and middle lobes on the right, which was biopsied and found to be an adenoma, according to Dr. Konzelmann. Because it was irremovable and because the patient had continuous symptoms of infection beyond the blockade, the lung was removed. This slide shows how large this tumor was. It also fungated through the bronchus, as did some of the adenocarcinomas described by Dr. Gebauer. This patient also made a good recovery and has recently been delivered of a nice child.

In brief then, let us say that we went over the last twenty-two cases of patients who had been explored, trying as best we could to apply Dr. Gebauer's standards, and we were able clinically to classify accurately about 65 per cent of the cases. We were more accurate in squamous than any other type, and I believe that corresponds to Dr. Gebauer's figures. I realize we were not applying his criteria as well as he would and possibly he could have called a higher percentage. It seems an excellent idea to be able to anticipate the histology of lung tumors from their clinical behavior. Calling our attention to group features such as these is a great contribution to our present literature.

DR. EVARTS A. GRAHAM, St. Louis.—Mr. President, I have so much I would like to say on this subject that I hope you will hold me rigidly to time and call me down.

I am always pleased when anybody attempts to simplify classifications, and I congratulate Dr. Gebauer for the attempt. My own feeling, however, is that he has not gone far enough, and I would also make one or two other points about his presentation; and, if there is time remaining, I would like to take the opportunity to show a few slides that concern what I think are important contributions to our pathologic conception.

Now, classifications are of value only if they enable us to have a better understanding of what the situation is all about. I am sorry that I will have to speak rather abruptly, because I want to get over a good deal of material.

I find it difficult—in fact, I find it impossible—to separate rigidly groups of small-cell carcinoma from adenocarcinoma. There are many tumors in which one finds a typical structure of adenocarcinoma alongside typical structures of what would sometimes be called small-cell carcinomas. It depends, therefore, upon what part of the tumor one selects from which to remove the tissue for examination.

Now, I have no hesitation whatever in agreeing fully with Dr. Gebauer on the idea that the squamous-cell carcinoma is a distinct type. That apparently comes from a metaplasia of the cylindrical epithelium, or at least from the basement layer of the epithelium. Moreover, its clinical characteristics readily set it apart from the other tumors. Its great predominance in men, its usual occurrence at a later age period, and other features are so well known that in 90 per cent or more of such cases it has been possible for one who has had a large experience to suspect that the lesion is probably a squamous-cell tumor if a bronchiogenic carcinoma seems probable in the presence of the various features just mentioned.

Then we come to a consideration of the origin of the other two classes which he has enumerated, and I think it is important to think of classifications as bearing on origin. I will say that this is a subject which Dr. Womack and I have been interested in for many years, six or seven years. We have examined a great many specimens carefully, and it is our opinion, for which I think we have a considerable amount of evidence, that the so-called small-cell carcinomas probably all come from a remnant of a bronchial bud which has been carried over from fetal life, but that, in the second place, probably all adenocarcinomas likewise come from the same origin, although there may be a few exceptions now and then which have an independent origin.

The importance of this conception, in my opinion, is that these remnants of the fetal buds are also the sources of the so-called bronchial adenomas. In our opinion, therefore—as I say, I cannot develop the line of thought in a few minutes—all bronchial adenomas are potentially malignant. It is, therefore, with jeopardy that one undertakes local removal of a bronchial adenoma. He may get away with it successfully occasionally and cure the patient of the trouble, but these tumors must be regarded, in our opinion, as potentially malignant.

Also these tumors have many characteristics identical with the mixed tumors which we see in the salivary glands. They are so nearly identical that oftentimes it is impossible to tell microscopically whether one is dealing with a mixed tumor of the bronchus or a mixed tumor of the parotid gland or of the submaxillary gland. We have submitted sections to many competent pathologists who are often unable to tell the source of the tumor, except that it is a mixed tumor. They often contain cartilage, sometimes pieces of bone, and so on.

These adenomas frequently resemble normal fetal tissue so closely that again it is impossible to distinguish between them. Normally, during fetal life, many bronchial buds are formed. All but about five of these, under normal circumstances, are supposed to atrophy and disappear, that is, in the human being. In some animals in which there are additional lobes, more remain. If one of these buds fails to

atrophy for some reason, it may remain latent for a great many years as typical fetal tissue indistinguishable from normal fetal tissue, and then because of some reason which is not clearly understood, it may begin to grow; and if it grows sufficiently, it will develop invasive qualities and become a malignant tumor.

Now, if there are a few minutes remaining, I would like to show a few slides.

I would like to say that anyone who is particularly interested in these views about which I am talking can find them more extensively developed in an article by Dr. Womack and myself in the *Archives of Pathology,* July, 1938.

(Slide) Here is one of these tumors which I would say exactly resembles the small-cell carcinoma grossly that Dr. Gebauer has mentioned. It also is identical with the structure which many people speak of as a bronchial adenoma.

(Slide) Here is a section through this tumor. You will see cartilage in this region, and here inside the cartilage are small areas of bone, and here is a larger area of bone. Around here, at the periphery, you will see what ordinarily might be designated as a small-cell carcinoma.

(Slide) Here is a high-power magnification of that part of the tissue.

(Slide) There is the lung removed. This was the lung of a woman 52 years of age, who had a tumor obstructing the bronchus at this point.

(Slide) I will call your attention to this microscopic slide here, and I would like to have you bear this in mind very closely. I will tell you that several competent pathologists called this an adenocarcinoma. Please bear this in mind.

(Slide) This is not another section of the tumor, but this is a section through a bronchial bud in a normal human fetus of sixteen weeks. Note the close similarity to the appearance of the tissue just shown.

(Slide) Here is a high-power magnification of this woman's tumor. Please keep this in mind.

(Slide) Here is a high-power magnification of the normal fetal lung of sixteen weeks, the low power of which you just saw. It is impossible to differentiate between them.

(Slide) Here is another one of these tumors. Now these tumors are frequently associated with congenital malformations. This occurred in a young man 17 years of age. He had no fissures, no lobules in the lung. A total pneumonectomy was performed.

(Slide) Here is a sample from one field. Shall we call it a small-cell carcinoma? Yes, if you wish. We prefer to think of these, however, as mixed tumors, because we think it is a more comprehensive term.

(Slide) Is it malignant? Well, you see a metastasis in the blood vessel. As a matter of fact, this young man survived operation, but a year later he developed evidences of cerebral metastasis, and I do not know whether or not he is still living.

(Slide) Here is another one of these tumors which we think of as mixed tumors, potentially malignant bronchial adenomas, if you will.

You will note a large number of accessory bronchi. As a matter of fact, there were seventeen different bronchi uniting this lung to the trachea, again an evidence perhaps of fetal abnormality which I think would tend to support the general idea. You can imagine also the consternation in removing this lung with constantly finding new small bronchial detachments.

(Slide) Here is a section of that tumor. What will we call it? Small-cell tumor or adenocarcinoma? What do you want to call it? I prefer to call it a mixed tumor of fetal origin in one of these fetal buds. That it is a malignant tumor is very evident from the invasive quality of the capsule which you see.

I am sorry I cannot go on any further.

DR. PAUL C. SAMSON, Oakland, Calif.—I had things all clear in my mind until Dr. Graham got up, and now I find myself confused again. On the other hand, I think that, by and large, the type of tumor Dr. Gebauer was talking about was not the type of tumor Dr. Graham was showing.

I might say, in preface, that some seven years ago I was working in Dr. Weller's laboratory, the pathologic laboratory at Michigan, and became interested in the autopsy studies of a large number of bronchiogenic carcinomas. It is with some pleasure that I hear some of my early views at least partially substantiated by Dr. Gebauer's paper.

In that group, about forty of which were studied personally and about sixty of which were taken from literature, we attempted to see whether there was any correlation between cell types—and I speak now of the three cell types which I still think are, in most cases, a pretty good differentiation; that is, adenocarcinoma, squamous-cell carcinoma, and the small round-cell carcinoma—and by means of mathematical formula, which is called the coefficient of correlation, we attempted to see whether those carcinomas of definite cell type tended to metastasize differently. The coefficient of correlation was picked instead of simple percentages, because each figure then gave us the tendency of a tumor to metastasize not only in relation to that particular cell type but in relation to the other cell types by comparison.

In brief, our findings were that the squamous-cell carcinomas—and this is on total autopsy material again, and not on clinical material—tended to metastasize late, if at all. They were locally invasive, involving adjacent mediastinal structures, pericardium, and so forth, really more direct extension than metastasis. Lymph node metastases, particularly distant lymph node metastases, were very rare. Metastases presumably of hematogenous origin, such as brain, kidneys, adrenals, and so forth, were rare.

The adenocarcinoma showed a tendency to metastasize widely, not only by lymph flow, but also hematogenously, so in the series of adenocarcinoma there were many metastases to the brain, kidneys, and so forth, and of course, many to the main lymph node cells of the body.

The small round-cell carcinoma, which many people in the past called sarcoma, showed a tendency to metastasize predominantly by lymph node involvement, with very little evidence in most of the cases of distant blood stream metastasis.

As a clinical application, of course, one can give a better prognosis prior to operation if a squamous-cell carcinoma is found.

Just in brief then, of six recent cases of carcinoma of the lung which have come to operation, four of them were of the squamous-cell origin, three having histories of nearly one year in duration, all operated upon, and none showing lymph node metastasis. Two were adenocarcinomas. I saw one very early adenocarcinoma that was operated upon within six weeks after the first symptom, and a small distal tumor showed microscopic lymph node metastasis. The sixth case, also adenocarcinoma of four months' duration, showed extensive metastasis to lymph nodes. The lung was removed, chiefly because it was a source of a great deal of infection. He survived eight months and died of generalized carcinomatosis.

I enjoyed this paper, and thank you for the privilege of discussing it further.

DR. ALFRED GOLDMAN, San Francisco.—First of all, let me express my appreciation of Dr. Gebauer's scholarly presentation of this subject. This question of the malignancy of bronchial adenomas and mixed tumors has interested us a great deal. We have had seventeen cases in our clinic and have reviewed the histology and histories of approximately fifty cases of adenoma seen in different parts of the country. So far, there has been but one in which metastasis to a lymph node was demonstrated. This case was one of Dr. Churchill's, and the tumor had no relation to a large bronchus. Dr. Castleman demonstrated the lone metastasis in an adjacent mediastinal lymph node. On the other hand, we collected fifteen cases (four from

our own clinic) in which the duration of the disease was more than fifteen years, without evident metastases. It seems to us, therefore, that the tumor which we recognize as bronchial adenoma is neither potentially malignant nor distantly metastasizing. We know of no case in which distant metastases have occurred.

Because of this, we fail to see why Dr. Graham should feel that this particular tumor is potentially malignant, unless its qualities, despite the absence of metastases, are considered sufficient to place it in that class.

We recognize, of course, that these tumors do grow beyond the bronchial wall and that they do produce pressure atrophy. However, in some which have reached the size of an orange, have destroyed a whole lobe, and have had a proved duration of more than twenty years, no metastases to lymph nodes occurred.

DR. GEBAUER.—I wish to thank Dr. Burnett. One case he showed of a small tumor arising in the left lower lobe, he also showed me before the meeting, and I thought it could be a benign adenoma, a primary adenocarcinoma or a primary small-cell carcinoma, or secondary tumor.

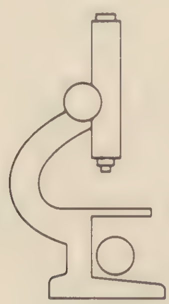
I agree with Dr. Graham that there is some confusion in differentiating between adenocarcinomas, bronchial adenomas, mixed tumors, and small-cell carcinomas. The criteria of the pathologist regarding malignancy and the criteria of most surgeons regarding malignancy are histologic, but the proof of malignancy is not the histologic picture; it is metastasis and invasion.

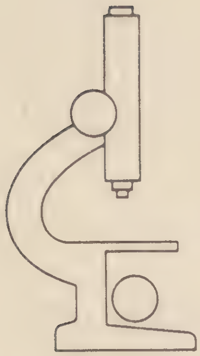
The only thing that prevents me from discussing it or trying to clear up the confusion is the fact that we have not seen many benign adenomas and mixed tumors. I would be pleased to have an opportunity to see these mixed tumors and benign adenomas and the small-cell carcinomas which simulate benign adenomas. We have seen a few benign tumors in which a biopsy may be misleading. The histologic field contains all the criteria for malignancy, with mitotic figures and wild growth, invasion of blood vessels, and so forth, but in the gross specimen the tumors are sharply circumscribed, there are no lymph nodes involved, and there seems to be no invasion at the periphery of the tumor.

As I say, I think the proof of malignancy is not the histologic picture as much as the end result, and I believe that we should treat these bronchial adenomas as potential malignancies (not necessarily completely radical), regardless of the fact that in seventeen cases there was only one, as reported by Dr. Goldman, that had lymph node metastasis.

I am familiar with Dr. Samson's work, and I was pleased to find mine confirmatory.

I would like to take this time to express my sincere appreciation for the helpful criticism and guidance of Dr. S. O. Freedlander.





TUBERCULOSIS

II. Treatment

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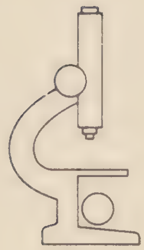
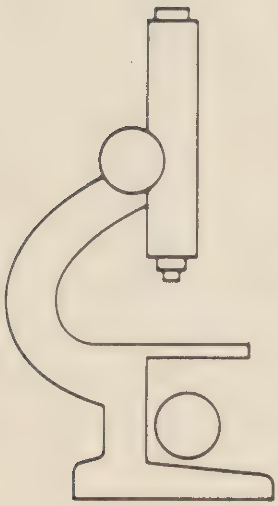


COLLAPSE THERAPY

SURGERY

EXPERIMENTAL THERAPY

REHABILITATION



COLLAPSE THERAPY

COLLAPSE THERAPY OF PULMONARY TUBERCULOSIS AND THE TREATMENT OF EMPYEMA

JOHN M. DORSEY, M.D.*

COLLAPSE THERAPY OF PULMONARY TUBERCULOSIS

The proved worth of the sanatorium in the treatment of tuberculosis is known to almost all. Less well known is the immense value of collapse therapy, especially when used in conjunction with the sanatorium regimen. From reliable statistics gathered in the careful study of an adequate series of patients it has been stated that as high as 85 per cent of those having pulmonary tuberculosis with cavity are dead in three years on sanatorium treatment alone. Yet we know that with the aid of collapse therapy, cavities have been closed in 75 per cent of cases in which it was used. Alexander states, "The surgeon's failure to do a minor revocable operation for so dangerous a disease as active early tuberculosis seems to me to be comparable to the failure to perform a prompt appendectomy for an acute attack of appendicitis on the ground that many attacks of appendicitis are known to subside under medical management."

Phrenic Nerve Interruption

Phrenic nerve interruption (Fig. 87, *A*, *B*, *C*) is designed to eliminate motion of the diaphragm on the homolateral side so as to allow for relaxation of the lung by reduction of the tension produced by the descent of the diaphragm. It has been the policy in recent years to interrupt the function of the hemidiaphragm temporarily by the crushing of one phrenic nerve (Fig. 87, *B*). In this way the diaphragm is paralyzed, may be elevated (*C*) and does not participate in respiratory motion for a period of three to five months, after which time its normal function returns without impairment.

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Technic.—The skin is prepared by cleansing with soap and water. About 5 to 10 cc. of 0.5 per cent novocain with adrenalin is used for local anesthesia. The incision is made on the selected side at a point 2 fingerbreadths above the clavicle, extending parallel to the clavicle laterally for about 2 inches from the outer edge of the sternomastoid muscle. It is best to mark the site of the incision with the back of the scalpel before introducing the local anesthetic. The skin, subcutaneous fat and underlying platysma muscle are incised and the few bleeding points secured by fine catgut. The superficial layer of the deep cervical fascia is carefully incised and spread by a dissecting scissors. The lateral border of the sternomastoid muscle is identified and a retractor placed under it, reflecting it medially. This forms the medial boundary of the *anatomic triangle* in which the phrenic nerve will be found. At a slight deeper level the omohyoid muscle is identified. It is reflected upward and serves as the upper and lateral boundary of the triangle mentioned, of which the lower boundary is the clavicle. The cervical fat is encountered in the center of this triangle and should be penetrated carefully by the use of blunt dissecting scissors. Care should be taken to avoid injury to the transverse cervical artery and vein in this region. Retractors are then used to expose the anterior scalenus muscle which lies in the depth of the triangle. A blunt curved retractor should be used to reflect the carotid sheath and its contained structures lying under the sternomastoid muscle.

The *phrenic nerve* is the only nerve running downward and inward in this region of the neck. It may be on, incorporated in, or under the fascia of the anterior scaleni muscle. For purposes of identification it is pinched by forceps. The patient will complain of pain over the point of the shoulder and may even be aware of diaphragmatic contraction. Once the nerve is identified it is infiltrated with 1 per cent novocain and crushed over a distance of 0.5 centimeter by a small mosquito forceps. It has been my policy to tie a fine black silk suture loosely about the phrenic nerve. It has been the experience of most everyone doing this procedure to fail to identify the phrenic nerve properly. If postoperative fluoroscopic study of the diaphragmatic motions does not show an

immobile diaphragm, re-operation is necessary. If such be the case identification of the previously marked structure is an aid to subsequent location of the phrenic nerve.

Indications.—Phrenic nerve interruption is successful as an adjunct to sanatorium rest in the cure of various types of tuberculous lesions for which rest alone is inadequate. Lesions which on bed rest alone either do not improve or increase in severity have been shown to respond after phrenic nerve interruption has been added. Since phrenic nerve paralysis produces less pulmonary relaxation than pneumothorax or thoracoplasty, it is more effective therefore in diseased foci which are neither extensive nor rigid. The primarily productive and early fibrotic types are most easily benefited.

Phrenic nerve interruption is used in unilateral or bilateral lesions even in instances in which there is a relatively small chance that it may be adequate in itself. Occasionally it is successful, but when it is not, further procedures, such as pneumothorax, may be added. When bilateral lesions are so treated, the temporary nature of the paralysis allows reversal of choice and the returning diaphragmatic motion on one side may allow for a similar paralysis to be tried on the opposite thorax.

Permanent phrenic paralysis is done primarily only in those patients who have so much of one lung destroyed that very little of it is of value in respiratory function, yet in whom the effect of the paralysis is of value. In those in whom one or more temporary paralyses have been beneficial, it may be necessary to produce permanent paralysis to maintain the benefit. It is dangerous to do primary permanent interruption otherwise, because a reduction in vital capacity may be produced which would prevent the use of a curative operative procedure later.

Phrenic paralysis is considered by some as being more effective in the control of *hemoptysis* than is pneumothorax. It is most beneficial as an adjunct to pneumothorax in patients whose lung and diaphragm are adherent. It serves well as a simple test of the contralateral lung when thoracoplasty is considered for the affected side.

The dangers of the operation are obviously those which

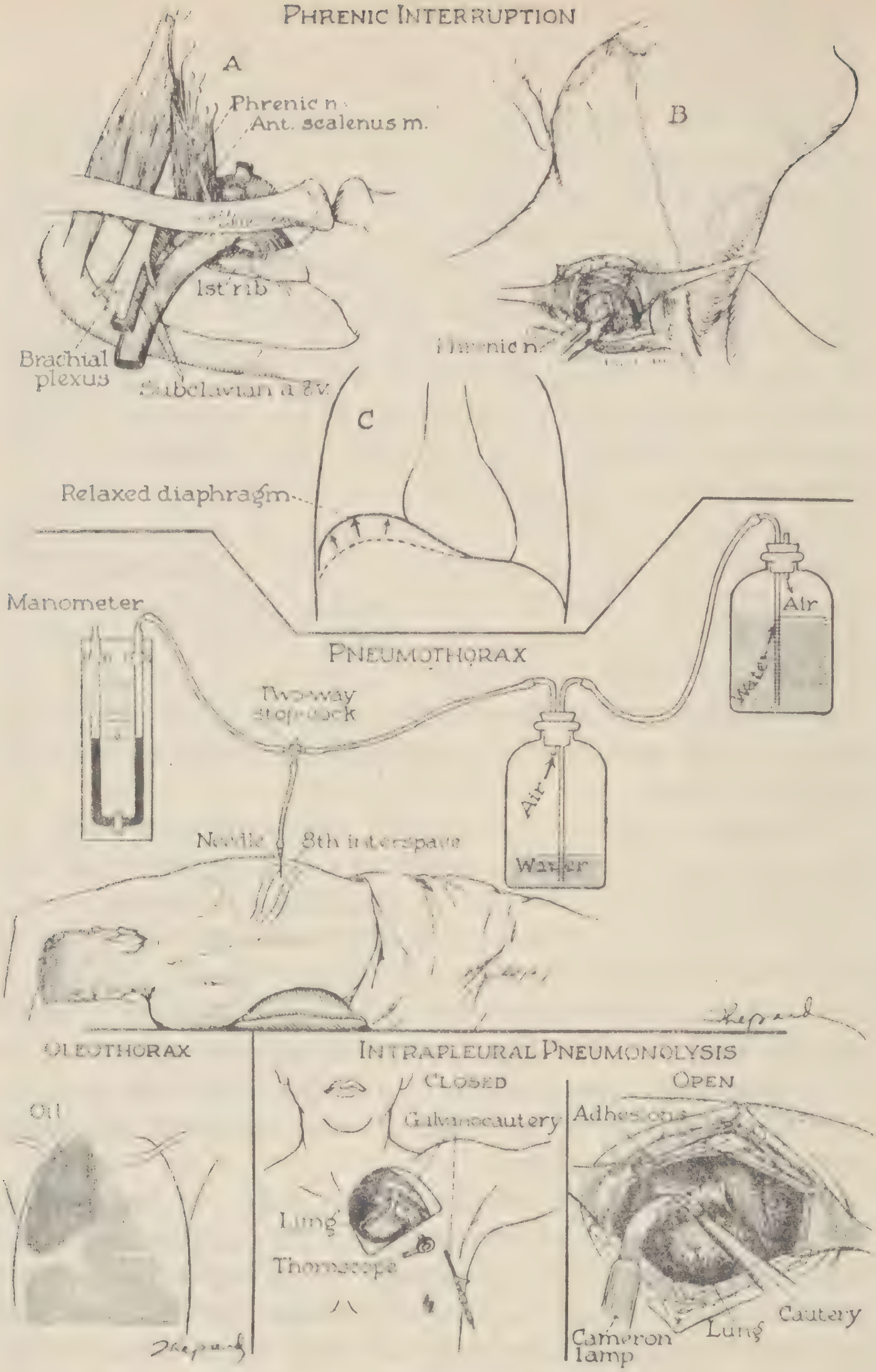

Fig. 87.—*Top*, Phrenic nerve interruption (see text).
Center, Pneumothorax (see text).
Lower left, Oleothorax. This is the introduction of oil into the pleural space applied to the treatment of pulmonary tuberculosis. Paraffin oil and

the anatomy of that portion of the neck entails.

Artificial Pneumothorax

Artificial pneumothorax (Fig. 87) or the introduction of measured amounts of air into the pleural space, is designed to relax the lung by the reduction of normal negative pressure which exists in the chest. Negative pressure is an expression of that cohesive force in effect between the visceral and parietal pleural layer. While these layers are in contact, the expansion of the chest wall on inspiration is transmitted to the lung within the thorax. When air is introduced between these layers, elastic recoil of the lung occurs by virtue of its elastic tissue construction. The negative pressure can be reduced and even changed to a positive pressure depending upon the discretion of the operator.

Technic.—Air can be introduced in the pleural space only when this space is free, that is, not obliterated by adhesions between the visceral and parietal layers. I prefer to use the eighth posterolateral interspace as the location of choice. Secondarily, the midaxillary line, and finally the anterior intercostal spaces may be tried if adhesions are encountered. The patient is placed in the recumbent position (Fig. 87), and the operative field is prepared with iodine and alcohol. A 10-cc. Record syringe with a Luer attachment is partially

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olive oil with or without gomenol are most often employed. They are injected through a needle and so replace the air of the pneumothorax for which they are substituted. The chief *indications* for the use of oleothorax are: (*a*) When there is danger of premature loss of pneumothorax because of an obliterature pleurisy; (*b*) when pneumothorax is complicated by the development of a chronic tuberculous infection of the pleura, especially a pure tuberculous empyema, which does not respond to simple measures of treatment.

Lower right, Intrapleural pneumonolysis. There are about 20 per cent complete failures in the induction of pneumothorax when undertaken, due to diffuse pleural adhesions. In approximately 45 per cent of cases, adhesions limit the collapse, and the partial pneumothorax produced is insufficient to permit healing of the lesion. Severing these adhesions may serve to produce adequate collapse. In the *closed* method under direct vision through a thoracoscope (an instrument with a lens system for inspecting the pleural space), introduced through a trocar, a galvanocautery unit is employed to divide the band as illustrated. In the more broad and diffuse adhesions, cautery division may be done through an incision opening the thoracic cage, in contradistinction to the closed trocar method. Since even the closed method of these procedures is dangerous, they should be undertaken only after simpler methods have failed, and by an experienced operator under proper conditions.

filled with 1 per cent novocain, using a long 24-gauge needle, a wheal is raised in the skin and the needle is slowly inserted down to the parietal pleura, injecting novocain ahead of it. Enough novocain is deposited outside of the parietal pleura to obliterate all pain sensation.

A short bevel needle of the pneumothorax type attached to the syringe is now inserted carefully through the parietal pleura. Novocain is injected in an attempt to separate the lung from the parietal pleural layer. The syringe is removed and needle attached to a manometer as indicated. If proper oscillations of the fluid in the manometer are obtained, air may be slowly injected. If, however, upon inserting the needle through the parietal pleura small air bubbles are obtained and no appreciable oscillation of the fluid level in the manometer is seen, then it must be assumed that the needle is in the lung tissue. Its point may then be withdrawn and the bevel shifted in direction in a further attempt to find free pleural space. Occasionally oscillations will be obtained when the needle is outside the parietal pleura. Injection of air will be quite painful and high positive pressure will be quickly built up. This will warn the operator that the pleural space has not been entered.

When it has been conclusively demonstrated that the pleural space has been entered, 250 to 300 cc. of air is injected. The patient is then examined fluoroscopically in the upright position and the air pocket is located. This procedure is repeated daily, adding 100 to 150 cc. amounts until a satisfactory pneumothorax is obtained or at least until the advisability of pneumothorax as a collapse therapeutic measure can be obtained. If satisfactory collapse of the lung can be produced in this manner, refills are carried out in the same region on each occasion. The frequency of refills will depend on the individual patient.

Indications.—Pneumothorax should be used in tuberculous disease which is *predominantly exudative* with or without cavitation where phrenic nerve interruption is likely to be inadequate. It is more useful in cavities whose walls are rigid with old fibrous tissue or whose size is such as to have a diameter of 3 to 4 cm. Pneumothorax should almost always be undertaken before thoracoplasty and other nonrevocable

collapse procedures, even though the likelihood of its success is not great.

If *dyspnea* is present in a patient on whom collapse therapy is undertaken, pneumothorax is preferable to phrenic nerve interruption, because if the reduction in vital capacity is intolerable the air may be immediately withdrawn. Pneumothorax is effective in *hemoptysis* for the control of hemorrhage when the location is known. It may be supplemented by phrenic nerve interruption, and in the presence of adhesions the collapse may be aided by the intrapleural severing of these bands (pneumonolysis).

Duration; Complications.—How long pneumothorax should be continued depends on the type of lesion, the patient's condition, and many other factors which are too varied to discuss in this clinic. It is well to bear in mind that there are complications which arise under pneumothorax therapy. Fluid may form in upwards of 50 per cent of patients under treatment. This may spontaneously absorb or go on to tuberculous empyema. There is then a diseased pleura in addition to a diseased lung. All of these things should prevent the indiscriminate use of pneumothorax by reminding the operator that whereas it is a valuable collapse method when indicated, experience with its usage is necessary to employ it for safety and success.

Extrapleural Thoracoplasty

The modern thoracoplasty operation (Fig. 88) consists in the removal of posterolateral as well as anterior rib lengths in several stages for the purpose of producing collapse of the chest wall and therefore of underlying pulmonary tuberculous lesions. This is a permanent or irrevocable procedure. When seven or eight ribs are removed we speak of "partial thoracoplasty."

Preparation of Patient; Anesthesia.—In general, it has been my policy to perform thoracoplasty under ethylene anesthesia which has been very useful in our hands for most thoracic surgical procedures. The patient is placed with the affected side upward (Fig. 87, under "Pneumothorax"), braced anteriorly by a Tudor Edwards support attached to the table. The head of the table is slightly lowered so as to

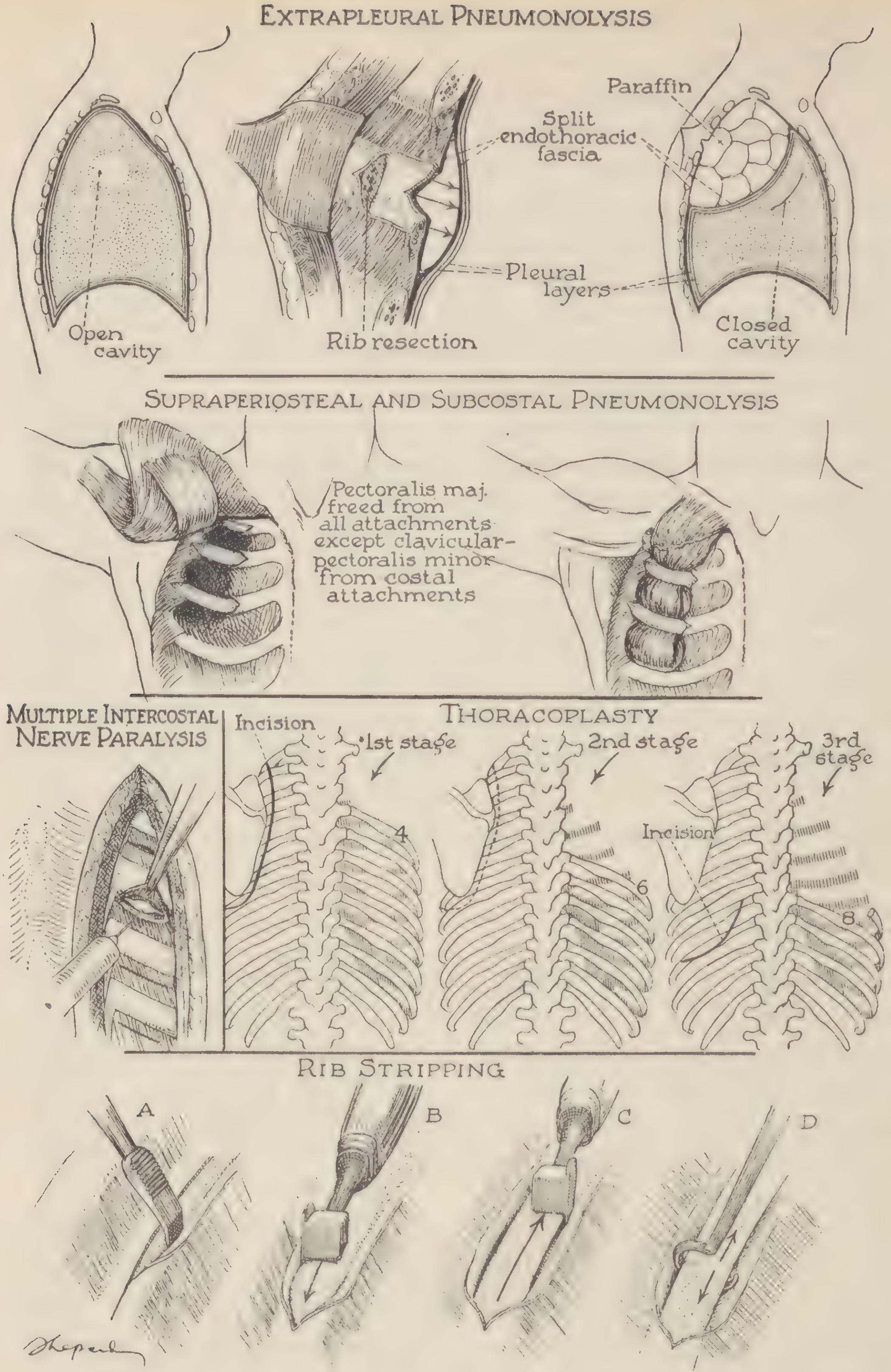

Fig. 88.–Extrapleural pneumonolysis. This is the freeing of the lung covered with visceral and parietal pleura from the overlying chest wall.

allow secretions to drain toward the mouth rather than be aspirated into the opposite dependent lung. Fluid is begun by administration through a cannula into a vein of the leg. Blood may be added to the system when needed. The skin is prepared carefully from the cervical region to the hip longitudinally and from the sternum in front to the lowermost portion of the thorax behind.

Technic.—The incision is illustrated in Fig. 88. The muscles of the thoracic wall between the vertebral border of the scapula and the spine are divided by Carter's method while being grasped between the fingers of the operator and his first assistant. Bleeding points are secured by forceps as they are cut across. In this fashion the latissimus dorsi muscles, the trapezius and the rhomboids are divided. The scapula is then retracted from the thoracic wall and maximum exposure is obtained by stripping the attachments of the serratus magnus muscle from their costal insertions. This allows for excellent exposure of the upper ribs. If in doubt as to the number of

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The separation is accomplished through the rib bed of a resected posterior portion of the third or fourth rib. A cleavage plane is developed between the endothoracic fascial and the parietal pleura. The space located is most usually filled with paraffin. Those few patients in whom phrenic nerve interruption and pneumothorax have failed, and who are poor thoracoplasty risks because of their general condition or because of extensive active lesions in the contralateral lung, may have their cavities collapsed effectively in this way.

Upper center, Supraperiosteal and subcostal pneumonolysis. In this operation the tissues are stripped away from the ribs over as wide an area as necessary. The space thus created is usually filled with muscle. Regeneration of ribs occurs from the stripped away periosteum at the new level. The *indications* are much as for extrapleural pneumonolysis. Cavities above the level of the clavicle anteriorly are not suitable for the procedure for apparent anatomic reasons.

Lower center, Intercostal nerve paralysis. Resection of the second to ninth intercostal nerves and the homolateral phrenic nerve reduces respiratory movement on the operated side approximately 80 per cent (Alexander). The illustration shows the injection with procaine through a vertical incision made parallel to the spine at the angles of ribs, preliminary to resection of the nerves. This operation has a limited application, namely (*a*) preparatory to thoracoplasty in patients in whom pneumothorax and phrenic nerve operation has failed and who are unsuitable thoracoplasty candidates at the time; and (*b*) in those patients with predominantly exudative lesions who would require thoracoplasty if intercostal neurectomy, being a less severe operation, did not offer a good chance of complete recovery.

Lower center, Thoracoplasty (see text).

Bottom, Rib stripping (see text).

ribs which might be safely resected in the first stage, the operator should primarily remove the second rib from its vertebral attachment to the costochondral junction anteriorly. This allows for adequate exposure of the first rib.

All ribs except the first may be resected by the maneuver of *stripping* (Fig. 88). The first rib presents more danger and more difficulty in its removal because of its surrounding important anatomic structures which are, from behind forward, the scalenus medius muscle, the serratus muscle, the brachial plexus, subclavian artery, tendon of the anterior scalenus muscle, the subclavian vein, tendon of the subclavius muscle, the heavy costoclavicular ligaments, and the fibers of origin of the pectoralis major muscle. It is obvious that a careful subperiosteal resection of the first rib must be carried out to avoid these structures which are in its proximity. The posterior portion of the rib is cut across and the anterior dissection is carried out by moving the rib backwards and forwards, held by a forceps, to allow for its best exposure. The anterior attachment is then severed.

It is important to point out the necessity for the *complete removal* of the ribs overlying tuberculous cavitation. This includes resection of the transverse processes which sometimes act as support, preventing adequate collapse of underlying cavities.

After resection of ribs, the wound is closed in layers without drainage. In this fashion the accumulation of serum adds to the efficiency of the collapse. It is seldom wise to remove more than three ribs at the first stage of the operation. The usual interval between stages is from two to three weeks. Second, third and fourth stages may be performed to remove as many as ten or eleven ribs. It is possible to do two stages through the incision indicated. A third stage in which ribs below the seventh are removed is best done through a separate incision (Fig. 88).

Postoperative Care.—In the postoperative care, careful attention is paid to respiratory efficiency; oxygen is used when necessary, and pain is controlled adequately but sedatives are not given in quantities sufficient to abolish an effective cough reflex.

Indications.—Thoracoplasty is used for patients who are

at least in fair general health, who have not had a recent exacerbation of their tuberculosis and whose cardiac and respiratory functional reserves are adequate. Tuberculosis with cavitation which is moderately or far advanced, mostly confined to one lung and productive in character, in such patients, presents the best indication for this operation; however, that is when pneumothorax or some other suitable operation has failed. There are many other considerations which govern the selection of thoracoplasty as a procedure of choice which are too detailed to mention in such a discussion.

Other Methods Employed in the Collapse Therapy of Tuberculosis

The less frequently employed methods of collapse therapy are illustrated and described in Figs. 87 and 88, where indications for their use are also given. These methods include *intrapleural pneumonolysis*, *oleothorax*, *extrapleural pneumonolysis*, *supraperiosteal and subcostal pneumonolysis* and *intercostal nerve paralysis*.

THE TREATMENT OF EMPYEMA

Empyema thoracis or suppurative pleurisy is a disease much more commonly found in children than in adults. Because the physiologic mechanism of the thorax, particularly when it is disturbed by a disease process, may be dangerously embarrassed, it has been recognized and proved by extensive experience that certain principles of treatment must be adhered to. The work of the Empyema Commission, headed by E. A. Graham, in World War I did much to elucidate these principles. In the main they are:

1. Careful avoidance of open pneumothorax in the acute stage of an empyema.

2. Prevention of chronic empyema by rapid sterilization and obliteration of the affected cavity.

3. Careful attention to the nutrition of the patient.

Certain other general statements should be made before discussing the actual technic and treatment. Graham has aptly stated that the mortality from the pneumonia causing empyema largely determines the mortality of the empyema itself. In other words, when pneumonia has occurred in relatively avirulent forms the treatment of the subsequent em-

pyema will be highly successful whether it be aspiration, closed tube drainage or rib resection and open drainage. Remembering this, it is understandable why the experience of some men leads them to advocate one or the other of these methods while a colleague may recommend another. However, when pneumonias are severe, then empyemas which accompany them are severe and only the best methods will stand the test of rigid trial. In planning treatment I like to consider empyema thoracis as an abscess confined to the pleura. As an abscess it needs adequate drainage. When one method fails to accomplish this it is necessary to resort to another. Sometimes it is necessary to employ the most radical method at once to avoid mortality.

1. Aspiration of the Chest (Fig. 89)

It is absolutely essential that the operator or surgeon about to aspirate a chest suspected of containing pus be entirely familiar with the roentgenographic appearance of pleural effusions. He must have before him anteroposterior as well as lateral views of the chest to be treated. The patient should be *sitting erect, supported by an assistant, who bends the patient forward and away from the affected side*, so as to widen the intercostal spaces selected for insertion of the needle. This is determined by correlation of roentgen observations with those of the physical examination, which is very important. Preparation should be made to perform this procedure very rapidly, particularly if the patient is quite ill.

I prefer to use iodine followed by alcohol for cleansing the skin over the area selected for aspiration. A 10-cc. Record syringe with a Luer attachment is filled with 1 per cent novocain solution. A wheal is raised on the skin with a hypodermic needle. A long 22-gauge needle is then used to anesthetize the thoracic wall in the intercostal location down to the parietal pleura upon which is deposited at least 2 cc. of the anesthetic agent. A larger needle is then fitted to the syringe and the needle is inserted into the pleural space.

The operator can detect the presence of thick parietal pleura and by constantly maintaining a slight pull on the plunger of the syringe will be able to observe pus flowing

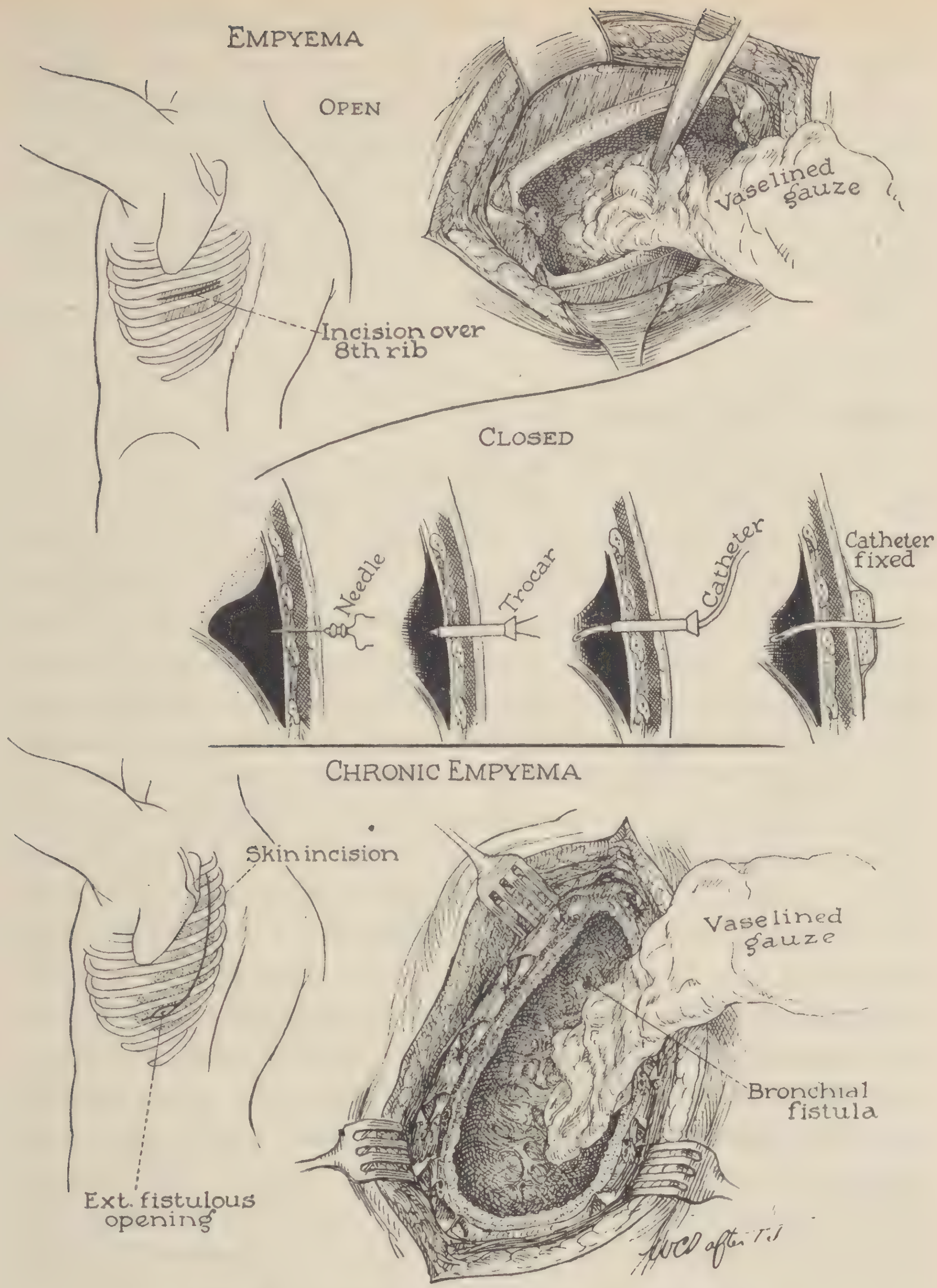


Fig. 89.—Technic of operations for empyema.

into the barrel of the syringe as soon as it is encountered. If thickened parietal pleura is not felt but rather small air bubbles return into the syringe, it is most likely that the empyema cavity has been missed and that the lung has been entered. Another site should then be selected. It is to be pointed out that even when thickened parietal pleura is posi-

tively identified, pus may not be obtained. *In this case a large bore needle should be substituted.* If thickened parietal pleura is felt and air freely flows back into the syringe, it is most likely that the space above a fluid level has been entered. This condition is produced in empyemas in which there is an associated bronchopleural fistula, either due to rupture of a lung abscess into the pleura or rupture of an empyema into the lung.

2. Closed Tube Drainage (Fig. 89)

Here again the patient is placed in the upright position for the reason described, and likewise everything must be in readiness for quick work. The operative field is prepared with iodine and alcohol, as in needle aspiration. *The empyema cavity has in all probability been located by previous needle aspiration.* If not, this is carried out again and it is advised that a large bore needle be used. Prior to this, anesthesia of the region through which the tube is to be passed should be obtained by infiltration of 1 per cent novocain solution, with about a 5 cc. quantity placed into the thickened parietal pleura. Although the position of the patient is the same as in needle aspiration, an attempt is made to further separate the ribs to allow for more ready access of a trocar, through which the tube is to be passed, without damage to the intercostal vessels. The trocar should be the largest one which the intercostal space will safely transmit. A small incision is made with the scalpel so that the trocar point may more readily penetrate the skin. Steady pressure is made on the trocar and pressure is made on the opposite chest wall by the assistant. The trocar point is then carefully inserted into the empyema pocket. There should be no plunging of an instrument of this nature haphazardly into a chest because of the real danger of damage to the underlying structures.

It is obvious to the operator when the empyema cavity is entered. This can be proved by withdrawal of the plunger which allows pus to flow from the tube attached to the dependent channel of the trocar. The largest catheter which the trocar will transmit is fenestrated in the portion which is to lie in the base of the empyema pocket. These fenestrations should not be so close as to interfere with the strength of the

catheter. The trocar is then withdrawn, leaving the catheter in place. The catheter is either sewn to the thoracic wall by a fishline silk suture passed through the wall of the catheter as it emerges from the chest, or a large safety pin is passed through the wall of the catheter through which adhesive strips are passed, fixing the catheter in place. Pus is withdrawn through the catheter to make sure that it is in working condition. It is unwise to withdraw large amounts of pus at one time, but in accordance with physiologic principles the cavity should be gradually decompressed. At the point where the catheter emerges from the skin of the chest wall adhesive tape may be used to unite closely the skin and the catheter to prevent leaking. Better yet, is to bring the catheter out through a 1-inch layer of sponge rubber which may be firmly bound to the chest.

If it has been determined that no bronchial fistula is present, irrigation of the empyema cavity should be carried out at regular intervals and after twenty-four hours normal salt solution, which is used at first, may be replaced with first 50 per cent Dakin's solution and finally full strength Dakin's solution. The position of the catheter in the cavity should be checked after twenty-four hours by roentgenograms of the chest. Regular irrigation of the tube will tend to keep it open and permit more successful results from this type of treatment.

There are two important points which need emphasis. First, a *bronchopleural fistula* may be known to be present by a fluid level in the pleural space that indicates communication with atmospheric air. Or the coughing up of sputum similar to that obtained by aspiration will suggest its presence and, finally, the tendency of a patient to cough violently on irrigation of empyema cavity and to taste irrigating fluid is conclusive.

Secondly, *how rapidly may a drainage tube be shortened?* This knowledge is gained from experience but the tendency is toward too early removal. As the lung expands and the cavity becomes decreased in size, the tube may be shortened. It is to be remembered that empyema cavities take from six to twelve weeks to expand completely. During this period the tube may be removed after the expanding lung has shown a tendency to extrude the tube spontaneously.

3. Open Operation

It is preferable that this operative procedure be carried out under 1 per cent novocain anesthesia supplemented by preoperative morphine sulfate and scopolamine hydrobromide or morphine sulfate and atropine sulfate. However, in children and in some adults we use ethylene gas by inhalation. *As in the preceding procedures, the empyema cavity is first located by needle aspiration according to the method described.*

The patient is then placed in the lateral recumbent position with the affected side up, leaving the needle through which pus has been obtained in place, but being careful that it is not broken off by action of the ribs when the patient is changed from a sitting to a lying posture.

The operative field is prepared with iodine and alcohol over an area larger than the surgical field. One per cent novocain with adrenalin is used to raise skin wheals and is then injected into the region of the under border of the ribs above and below the ribs selected for resection. A quadrilateral area demarcating the limits of the operative field is then infiltrated with 0.5 per cent novocain containing adrenalin. The line of incision over the rib selected for resection adjacent to the needle is infiltrated down to the periosteum of the rib. Incision is made through the skin and thoracic musculature and retractors placed so as to expose the rib in question. One per cent novocain is then used to raise the anterior periosteum of the rib. This is incised and reflected back as illustrated (Fig. 88, under "Rib Stripping"), exercising care not to injure the intercostal vessels which lie in the intercostal groove on the under surface of the rib. A 2-inch segment of rib is resected with the double-action Stille rib shears. A large bore needle is then inserted through the posterior periosteum and parietal pleura to further assure the operator that he is over the empyema cavity.

The cavity is now opened over a distance wide enough to admit the index finger so that the cavity may be explored and its limits determined. *This is to allow for the resection of the correct lengths of ribs which overlie the cavity, the removal of which will allow for its most adequate drainage.*

This is a very important step as far as the success of the treatment is concerned, particularly regarding the postoperative care of the wound. The cavity is then evacuated of its pus by suction aspiration. Fibrin clots are removed by hand or, if no bronchial fistula exists, by irrigation with saline solution. Here it is worth while stating that *never should adhesions between the lung and chest wall be disturbed*. The pillars of lung tissue are important to the re-expansion of the lung in the presence of an open pneumothorax. They prevent the consequence of open pneumothorax which have been emphasized previously, namely respiratory failure. The rib ends are cut well back of the edges of the empyema cavity, leaving them smooth and not jagged. They should be left protected with periosteum so as not to be later involved by osteomyelitis. Two ribs are ordinarily resected in this manner (Fig. 89) and the intervening intercostal bundle with the intercostal vessels and the thickened parietal pleura are removed, after first ligating proximally and distally with heavy catgut.

The cavity is now packed widely open with a broad roll of sterile vaseline gauze, and the soft tissues of the thoracic wall are thus prepared and held in an elliptical-shaped opening by this packing. This is very important as regards the subsequent care of the wound. The gauze is removed in forty-eight hours. This procedure is painful and the patient should be given morphine or codeine in advance. The cavity is irrigated with a *measured* amount of normal saline solution which is then withdrawn. The cavity is packed widely open again with wide gauze soaked in normal saline solution. After four or five days of daily dressing the saline solution is replaced first by 50 per cent and then full strength Dakin's solution. This dressing is carried out daily until the cavity has been obliterated.

It may be necessary to do *plastic procedures* on such a wound to enable the operator to pack it under direct vision until it is healed. This is one of the most important steps in this method of treatment. A patient who has been ill with pneumonia and empyema may be gotten out of bed within a few days after operation because it is the most satisfactory

way of bringing about a normal temperature. If temperature persists, it is a sign that either adequate drainage has not been obtained or that another process is present. Careful follow-up x-ray pictures should be made at intervals.

Treatment of Chronic Empyema

It is necessary to obtain *adequate drainage* as a first step in the treatment of chronic empyema rather than to precede with any major collapsing operation, because rather large chronic empyema cavities may be considerably reduced in size by the institution of adequate drainage, leaving a much less radical procedure to eliminate the residual cavity.

Adequate drainage may be obtained by means of a tube over which has been placed a nicked finger cot, after the method of Lilienthal. On coughing or straining the pus will be forced out but on inspiration the finger cot collapses and prevents the inspiration of air.

I prefer a modification of the operation proposed by the late Major Keller of the Walter Reed Hospital in the treatment of chronic empyema (Fig. 89). It is necessary that the patient's blood be typed and available donors be on hand because the operation may be shock-producing. The residual chronic empyema cavity has been previously visualized by injection of opaque oil into the sinus and anteroposterior and lateral roentgenograms taken to demonstrate the limits of the cavity. Resection of the thoracic cage overlying the cavity at its most dependent portion is begun by widening the sinus tract. All of the overlying ribs are resected so as to expose completely the cavity when the thickened parietal pleura beneath the ribs is removed. This is dissected away after first transfixing the intercostal vessels with heavy chromic catgut sutures both proximally and distally. The cavity thus prepared is cleansed, curetted if necessary, and all pockets opened and packed with vaseline gauze as described earlier under "Open Operation." This is allowed to diminish in size by the natural healing process under direct vision. Plastic procedures may be necessary from time to time to do this satisfactorily.

PNEUMOTHORAX TREATMENT OF PULMONARY TUBERCULOSIS[1]

Results in a Follow-up Study of 117 Cases

ALLAN HURST AND SOLOMON SCHWARTZ

Though begun about sixty years ago, pneumothorax therapy in pulmonary tuberculosis did not become a popular procedure until more than thirty years later. During that time, there has been an advance in knowledge as to indications, particularly in the so-called progressive minimal case, as well as in bilateral cavitary disease. After the treatment has been continued satisfactorily for some years, the problem arises as to the optimum time for discontinuation. There is complete lack of agreement in this regard, for various investigators suggest markedly different periods. Neumann (1) has suggested a collapse lasting two years, and others recommend that the treatment be continued indefinitely. Some recent workers insist that the duration of the treatment depends upon the character and extent of the original lesion with a minimum collapse of five years.

There have been few reports in the literature in regard to end-results of pneumothorax therapy. In addition, most investigators have included cases with ineffective collapse which were discontinued very early in the course of therapy. Because of the improper inclusion of these cases, there has resulted considerable confusion.

OBSERVATIONS

The present study consists of 117 pneumothorax cases, all of whom have had collapse therapy for a minimum of two years. In a small group, a little less than 10 per cent, the treatment was discontinued involuntarily. They have been included however, because they conformed to the minimum length of therapy. All cases were treated in two of the large Department of Health Clinics in New York City. They were previously treated in the tuberculosis sanatoria and hospitals of New York State for the most part where they remained for at least six months.

[1] From the Bureau of Tuberculosis, Dr. Herbert R. Edwards, Director, Department of Health, New York City.

On admission to the clinic, they were considered to be cases of effective collapse, that is, the sputum had been rendered negative. The patients were almost invariably of quite low economic levels, many living on subsistence diets.

In the clinic, the pneumothorax was continued at regular intervals and examinations and X-ray films were done periodically. Sputum studies, both by concentrated method and by gastric lavage were done frequently, particularly just before and after cessation of therapy. About two years ago, the use of the erythrocyte sedimentation test was discontinued. Work done by Pessar and Hurst showed that there was too great a discrepancy between sedimentation rate and clinical condition of the patient, as determined by X-ray, weight, temperature and work ability, to warrant much reliance to be placed upon it.

In only a little more tha two-thirds of the cases were we able to secure the original X-ray films prior to the institution of collapse therapy. In the remainder we were forced to accept a description of the X-ray findings forwarded to us from the sanatoria and hospitals.

After it was decided to discontinue a case, pneumothorax refills were stopped abruptly. Each was watched carefully with frequent X-ray examinations and sputum studies during the reëxpansion period. In many, small pneumothorax pockets and other highlights appeared which were difficult to distinguish from cavities. When these were seen, we had to rely upon the results of serial X-ray films and sputum examinations for final decision. In no instance was it necessary to resume the pneumothorax treatment during reëxpansion because of suspicious X-ray shadows.

For convenience, we have grouped our cases, insofar as their present status is concerned, into "dead," "active," "arrested" and "apparently cured." The last three named will be defined to avoid misunderstanding, although we have attempted to stay as close as possible to the definitions of the National Tuberculosis Association.

Active: Any case showing a positive sputum or unstable lesion by X-ray. Where patients showed significant symptoms without X-ray changes, they were carefully observed until a definite diagnosis of activity could be made.

Arrested: Following complete reëxpansion, a negative sputum, a stable lesion by X-ray, no significant complaints and a fair degree of physical activity for a minimum of six months. Because of the question of physical activity, many cases have been included in this group who would

otherwise be added to the last, apparently cured group, because of their inability to work. For the most part, this has been due to dyspnoea on exertion, an end-result of the retraction and pulmonary fibrosis following pneumothorax therapy. Similarly, 4 cases of localized tuberculous empyemata have been added although they fit into the cases of cured by definition.

Apparently cured: Following discontinuation of pneumothorax, negative sputum, stabilized lesion on X-ray, and the ability to work for not less than two years.

In discussing our results, we have grouped together the dead and active cases, for comparison with the total of arrested and apparently cured cases. The average follow-up of all cases, except those dead or in a hospital since discontinuation of therapy, was four years. The minimum was one and one-half years, and the maximum six years and two months.

TABLE 1

Present status of cases according to duration of pneumothorax

STATUS	DURATION OF PNEUMOTHORAX								
	2 years		3 years		4 years		5 years and over		Total Cases
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	
Apparently cured	14	63.7	45	65.2	15	75.0	5	83.3	79
Arrested	3	13.6	9	13.0	4	20.0	—	—	16
Active	5	22.7	14	20.3	1	5.0	1	16.7	21
Dead	—	—	1	1.5	—	—	—	—	1
Total	22	100.0	69	100.0	20	100.0	6	100.0	117

Age: The youngest patient was sixteen, and the oldest fifty-eight years of age. The greatest number of cases were between twenty and thirty years of age. We were unable to find any difference in the incidence of breakdowns in any particular group.

Sex: There were 53 males and 64 females. Again the incidence of breakdowns was not remarkably different in the two series.

Race: Since the majority of the cases (109) were of the white race, it was impossible to draw any comparative conclusion.

Duration of pneumothorax is best shown in table form. The duration of pneumothorax in years has been plotted against the present status of the individual case. There will be a slight variation in the figures as

compared with those shown later in the table of relapsed cases. This is due to the fact that in table 1 we are discussing the present status, and a few of the relapse cases have since become arrested or cured.

There were 12 cases of pneumothorax expanded involuntarily that are included in the series. They were divided as follows:

a: Obliterative pleuritis: 5 cases. Length of pneumothorax was from two to three years and all are apparently cured.
b: Massive effusion: 2 cases. Pneumothorax of two years' duration. Both cases had contralateral breakdowns, one of whom is active and the other arrested.
c: Delinquency: 4 cases. Pneumothorax was continued for a little over two years to more than four years. Of the 4 cases, 2 are arrested, one is apparently cured and one is active with a homolateral breakdown.
d: Temperature reaction: one case. Length of collapse was more than three years and the patient is apparently cured.

Duration of the disease by symptoms prior to institution of pneumothorax was analyzed as to results of therapy. Symptoms of less than six months, from six to twelve months and more than one year were compared. It was surprising to find that the incidence of breakdowns was least in those having symptoms for more than one year. It would appear from this that the more chronic the case, the better the results from therapy, once a good collapse is secured.

The interval of conversion of sputum was similarly studied. Here the various classes were charted against conversion groups of less than three months, from three to six months and more than six months. The comparison of these three groups showed little or no difference in the end-result. It may be concluded that once the collapse becomes effective enough to render the sputum negative, the result is uniformly the same regardless of the time interval.

Probably the most important single factor of pneumothorax is the character of collapse as influenced by adhesions. For convenience we divided our cases into three groups as follows (this represents a modification of the four groups of Hjaltested and Törning (2):

1: No adhesions to apex or costal wall. Mediastinal or diaphragmatic adhesions were not included since we had no cases of basal cavity.
2: Circumscribed or isolated apical or costal adhesions, also called "band" or "string" adhesions.
3: Diffuse pleural symphsis or multiple costal adhesions.

In other reports on the results of pneumothorax therapy, the character and extent of the original pulmonary lesion was that of the National Tuberculosis Association. We have divided our cases, as seen in table 3, into unilateral and bilateral. Under bilateral, they have been further subdivided into significant and insignificant lesions. An insignificant lesion will be defined as a small fibrotic nodule or strand, or calcifications

TABLE 2

Present status of cases grouped according to character and extent of adhesion

STATUS	GROUP 1		GROUP 2		GROUP 3		TOTAL CASES
	Number	Per cent	Number	Per cent	Number	Per cent	
Apparently cured	22	81.5	42	66.7	15	55.6	79
Arrested	2	7.4	9	14.3	5	18.5	16
Active	3	11.1	11	17.5	7	25.9	21
Dead	—	—	1	1.5	—	—	1
Total	27	100	63	100	27	100	117

TABLE 3

Present status of cases according to character of original lesion

STATUS	UNILATERAL		BILATERAL				TOTAL CASES
			Significant		Insignificant		
	Number	Per cent	Number	Per cent	Number	Per cent	
Apparently cured	44	71.0	29	65.9	6	60	79
Arrested	11	17.7	4	9.1	1	10	16
Active	7	11.3	10	22.7	3	30	20*
Dead	—	—	1	2.3	—	—	1
Totals	62	100	44	100	10	100	116*

* One active case is excluded from total, as pneumothorax was induced in a foreign country and original X-ray findings could not be secured.

at the apex or localized in the lung, recognized as other than a healed primary infection.

Relapses: These will be discussed separately under relapses occurring on the side of the pneumothorax, homolateral, and those on the opposite or contralateral side.

There were 12 cases of homolateral relapse in the series of 117 cases, or approximately 10 per cent. Of the 12 cases, 3 relapsed after six months, 4 after one year and 6 after more than two years. As to the duration of pneumothorax, the best results were secured in the group with

pneumothorax for more than four years. Two became active in the two-year group, nine in the three-year group, and only one in the four-year group. In the study made for the type of lesion found in the homolateral relapses, we could only use 11 of the 12 cases, because one had had her pneumothorax induced in a foreign country and we were unable to secure the original X-ray films. There were 6 unilateral and 5 bilateral cases. As to the character of collapse, it is to be noted that there were no relapses in the ideal group 1. There were 7 relapses in group 2 and 5 in group 3.

Relapses were diagnosed on the basis of increasing symptoms, X-ray changes or positive sputum. Among these 12 cases, we have included one case that developed an empyema two years after reëxpansion. He subsequently had a thoracoplasty and is now arrested.

TABLE 4

Present status of all relapsed cases

	APPARENTLY CURED	ARRESTED	ACTIVE	DEAD	TOTAL
Homolateral		3	9		12
Contralateral	2	2	12	1	17

In the contralateral group, there were 17 cases. Of these, the majority of relapses were in the nature of small exudative lesions which could be treated by simple rest regimen. We have not included those contralateral lesions which were a problem during pneumothorax therapy since we are dealing only with results following reëxpansion. The interval of breakdown was not extraordinary in any time grouping, since about equal numbers were found from six months up to three years after reëxpansion.

COMPLICATIONS

There were 2 cases of rheumatic heart disease, both of whom went through their pneumothorax therapy satisfactorily. Three cases of diabetes mellitus, all well controlled by diet and insulin, were successfully treated and are in the apparently cured or arrested group. Five patients became pregnant during pneumothorax therapy and delivered without mishap. One of these 5 also went through a pregnancy following re-expansion. All 5 cases with 6 pregnancies are well. One other patient became pregnant after reëxpansion and reactivated her pulmonary lesion after reëxpansion one year after delivery.

Although not a complication, it is to be noted that in the series of

117 cases, there were 3 cases with bilateral pneumothorax, all well and in the "apparently cured" group.

There were 4 cases of localized tuberculous empyemata which were discussed previously. These patients are all working and really belong in the "apparently cured" group by virtue of definition. They have been placed in the "arrested" group to avoid criticism, although we feel that the pulmonary lesion is well healed, and the small collection of pus is the remains of a burned-out infection and does not represent a therapeutic problem.

There was one case of haemothorax and 11 cases of massive *ex-vacuo* effusions treated conservatively for the most part.

Bronchiectasis was demonstrated with lipiodol in 4 cases, although we feel that there were probably many more cases.

Under adjuvant procedures, there were 2 thoracoplasties, one for a contralateral lesion, and one for empyema on the homolateral side mentioned previously. There were also 3 phrenic nerve operations, and 4 cases of intrapleural pneumonolysis.

DISCUSSION

It has been estimated that the 117 cases here discussed represent about 1,000 cases of pulmonary tuberculosis in institutions for whom pneumothorax was originally planned. Of these 1,000 cases, only 25 to 30 per cent will be satisfactorily induced. Massive effusions, empyema, progressive tuberculosis and other complications will eliminate many more. After discharge from the hospital and sanatorium, similar complications, as well as obliterative pleuritis, will again bring the total down markedly. Thus it must be emphasized that we have discussed here the results of the "good" cases, arrived at by a so-called "self-weeding" process. Viewed from this light one would have expected far better results.

There are still advantages of a successful pneumothorax as compared to conservative methods of treatment. Only one of our patients is dead and the remainder are alive, an average of seven years after induction of pneumothorax. Similarly Eglee and Jones (3) had only one death in 100 reëxpanded pneumothoraces followed an average of 3.2 years. Half of 20,000 open cases were dead in five years (Berg (4)). Barnes and Barnes (5) found that the average duration of life of positive sputum cases was thirty months.

Patients in whom pneumothorax has been tried and failed have a very high mortality rate. Packard (6) found a mortality rate of 60 per cent

at the end of two years in patients in whom pneumothorax had been tried unsuccessfully. Sinding-Larsen (7) had a mortality rate of 22 per cent in 142 pneumothorax failures. In contrast, Peters *et al.* (8), Packard (9) and Sinding-Larsen (7) had a mortality rate of 11 per cent or less in effective pneumothorax cases.

A problem in pneumothorax therapy is when to discontinue pneumothorax. Packard's (9) best results were in pneumothorax maintained two years or more. Dufault and Laroche's (10) best results were in pneumothorax maintained for over three years. Our figures show a sharp dividing line once pneumothorax is maintained for four years or more. Of 20 cases who had pneumothorax maintained for four to five years, only one is active. We do not feel that a contralateral relapse can be attributed to or explained by a pneumothorax. Of 12 homolateral relapses only one occurred in a patient who had a pneumothorax maintained for four to five years. This would suggest that pneumothorax maintained for a period of at least four years should produce a more favorable outcome, with fewer relapses than one maintained for a shorter period.

We did not find any particular difference in the end-results of young or old patients, in female or male patients, or between a short history or a long history of disease. Our length of disease was determined by symptoms, although, of course, this is not reliable. Veran (11) had found that the shorter the duration of the disease, the higher the percentage of cures and the fewer the relapses.

One important difference in our figures is noted in comparative results in unilateral and bilateral cases. Thus 7 out of 62 unilateral cases are active at the present, as compared to 13 out of 54 bilateral cases. This indicates the importance of an early diagnosis and the institution of collapse therapy before the case has become bilateral. All contralateral lesions are potentially dangerous.

The end-results were superior in pneumothorax induced for patients without cavities. Only one is at present active out of 23 such cases. We could not demonstrate that cavity size played a part. There is no necessary relation between size of cavity and tissue destruction since physiological variations in size may be due to bronchial changes. The question of an early induction of pneumothorax for a lesion without cavity but with positive sputum is an important one to be considered. The outcome is favorable in our group but whether bed-rest would have given as good results with the noncavernous cases is uncertain. Barnes (12) found 40 per cent of noncavernous cases with positive sputa dead

in three years after conservative treatment. Pneumothorax is not innocuous, as Pinner, Leiner and Zavod (13) have shown by bronchospirometry that the reëxpanded lung though appearing intact may be functionally disabled.

The study of relapsed cases brings out several important points. It is impossible to forecast the outcome of any case until a long enough period of follow-up has been obtained. For instance, we note that most of our cases showed relapses more than one year after discontinuance. This is especially true in cases of homolateral breakdown where pneumothorax played a real part. It is interesting to note that only in one case has a breakdown occurred in the 26 cases which have been followed now for four years or longer after expansion. In other words, a breakdown will occur ordinarily from one year to three years. This suggests that a follow-up should be fairly intensive with periodic X-ray and sputum check, every three months, for at least a three-year period, and only after three years can one relax observation.

We do not feel that the existence of pneumothorax on one side had any particular effect on the contralateral lesion, but that the contralateral lesion pursued its evolution depending upon its character, whether productive or exudative.

The character of the collapse seems to us to be of prime importance in the outcome of the disease. Where the pneumothorax was perfect, that is, without adhesions (group 1) our figures show no relapses on the homolateral side, whereas 12 relapses occurred in groups 2 and 3. One should therefore try to obtain as perfect a collapse as possible, even if sputa are negative and no cavities are seen. No cases with perfect collapse showed reactivation in the homolateral lesion.

We feel that, if pneumothorax is not to fall into disrepute due to frequent reactivation, one should not remain satisfied with conversion as a criterium for good results but, rather, an anatomically perfect collapse should be obtained.

There has been considerable difference of opinion as to the method of reëxpansion. Dundee and others gradually prolonged the interval of pneumothorax until the lung had totally expanded. Our pneumothorax refills were stopped abruptly. This did not seem to predispose toward massive effusion of which we had 11 cases. Fluid usually accompanying pneumothorax was spread over the surface of the expanding lung and appeared larger than it actually was. None of our cases showed relapses on the pneumothorax side until at least one year after cessation. We

do not see any particular point in the method of gradually allowing the lung to expand, as most relapses will occur sometime after the lung has completely expanded. We did not observe any case that showed re-opening of a cavity or recurrence of a lesion, immediately on expansion. Therefore, no lung required immediate recollapse.

This is important because very often as the lung reëxpands, many pseudo-cavity ring shadows are formed by local pleural thickening, areas of fibrosis, areas of emphysema and small, pocketed pneumothorax and hydropneumothorax. Consequently, although one naturally watches the lung carefully as it reëxpands, one cannot prognosticate the outcome by what one observes at this time. Rarely was it found necessary to withdraw any fluid which formed at the time of reëxpansion, since it did not seem to cause symptoms, although it did sometimes interfere with perfect visualization of the lung.

SUMMARY AND CONCLUSION

1. We have reported 117 cases of abandoned pneumothoraces, all of whom have had collapse therapy for at least two years.

2. These cases have been followed since discontinuance for an average period of four years.

3. Of these 117 cases, at present, one is dead, 79 apparently cured, 16 arrested and 21 active.

4. There were 12 homolateral and 17 contralateral relapses.

5. Contralateral disease has a definite deleterious effect on the outcome of reëxpanded pneumothorax cases so that cases of bilateral disease have a more serious prognosis than those of a unilateral disease.

6. The best results were observed in cases with at least four years of pneumothorax.

7. Abrupt cessation of refills and careful watching of the lung as it reëxpands is preferable to gradual reëxpansion of the lung.

8. Early pneumothorax in positive sputa cases is indicated regardless of the absence of cavity.

9. Best results are observed in cases with ideal collapse, that is, without adhesions to apex or costal wall. Therefore, early Jacobaeus operation should be considered in cases with adhesions, even though the sputa are negative.

10. Final outcome in reëxpanded pneumothorax cases cannot be ascertained until at least three years after reëxpansion.

11. Although ultimate results are not as favorable as immediate results

in pneumothorax, pneumothorax treatment seems preferable to conservative methods of treatment in positive sputum cases.

REFERENCES

(1) NEUMANN, W.: How long should an artificial pneumothorax be maintained, Wien med. Wchnschr., 1936, *86*, 1129 and 1167.

(2) HJALTESTED, O., AND TÖRNING, K.: Clinical aspects of pneumothorax therapy, Brit. J. Tuberc., 1939, *33*, 1.

(3) EGLEE, E. P., AND JONES, O. R.: A review of 100 reëxpanded cases of artificial pneumothorax, Am. Rev. Tuberc., 1937, *35*, 500.

(4) BERG, G.: The prognosis of open pulmonary tuberculosis, Acta tuberc. Scandinav., Supplement IV, 1939.

(5) BARNES, H. L., AND BARNES, L. R. P.: The duration of fatal phthsis, Am. Rev. Tuberc., 1929, *20*, 895.

(6) PACKARD, *et al.*: Artificial Pneumothorax, Lea & Febiger, Philadelphia, 1940.

(7) SINDING-LARSEN, C. M. F.: Collapse treatment of pulmonary tuberculosis, Acta medica Scandinav., Supplement 80, 1937.

(8) PETERS, *et al.*: Survey of artificial pneumothorax in representative tuberculosis sanitoria, Am. Rev. Tuberc., 1935, *31*, 85.

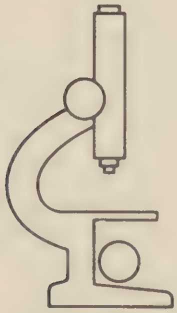
(9) PACKARD, E. N.: Present status of 100 pneumothorax patients after 1–18 years expansion of lung, J. Thoracic Surg., 1932, *1*, 581.

(10) DUFAULT, P., AND LAROCHE, A.: Question of when artificial pneumothorax should be discontinued, Am. Rev. Tuberc., 1935, *31*, 139.

(11) VERAN, P.: La cessation du pneumothorax artificiel, Doin et Cie, Paris, 1932.

(12) BARNES, H. L.: The prognosis of noncavernous phthsis, Am. Rev. Tuberc., 1933, *28*, 660.

(13) PINNER, M., LEINER, G. C., AND ZAVOD, W.: Personal communication.



ARTIFICIAL PNEUMOTHORAX

A Nonstatistical Analysis of the Major Factors Involved in Its Proper Management

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ARTIFICIAL pneumothorax is the most widely used of all surgical procedures for the control and treatment of pulmonary tuberculosis. Among those experienced in its use there is almost unanimous agreement that, judiciously applied, it is of great value, in spite of the fact that in recent years several statistical studies[1, 2, 3] have been loosely interpreted as indicating that collapse therapy in general does not improve prognosis. On the other hand, it is true that no one can say exactly of how much value it is; this question may prove to be extremely difficult to answer because of the particularly complex and protean nature both of tuberculous disease and treatment. Indeed, when a statistical solution to the question was attempted in England a few years ago,[4] it became apparent that a completely sound approach from this standpoint could not be made. The factors which account for this difficulty are well recognized and need not be commented on here.

However, if accurate knowledge cannot be gained from mass studies of this sort, there is, nevertheless, a line of investigation on the subject which can be of great importance. This is concerned with the effort to make certain that when pneumothorax is used, it is used properly and in accordance with recognized modern principles. By its very nature, pneumothorax admits of countless variations in application and it is axiomatic in surgery that results of any therapeutic procedure depend primarily on the way it is used. A survey of the literature and texts on tuberculosis reveal that remarkably little attention has been given to details of management of pneumothorax; in fact, the implication carried in many of these articles is that it is the mere act of administering pneumothorax, rather than the way it is administered, which determines prognosis. It has been our experience, and it is the premise upon which this discussion is based, that results with pneumothorax do vary greatly with the way it is used, that there are right ways and wrong ways of applying it, and that, for this reason, its potential value will be fully realized only when it is conceived as a much more exact procedure than at present.

There are several distinct aspects of pneumothorax and the management of each should be governed by definite objective principles. It

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is the purpose of this discussion to outline these aspects and to describe, as concisely as possible, the various factors which we think contribute toward a more rational understanding of the procedure. Some of these are the result of recent technical developments (pneumonolysis, bronchoscopy), some are the result of analysis of our own past mistakes, and others are the result of applying to pneumothorax some ordinary sound surgical principles and a long-range viewpoint.

Among the basic aims of management are (1) the reduction of complications to an absolute minimum, and (2) the differentiation, as early as possible, between an effective and an ineffective pneumothorax. Neither of these is attainable unless surgical aid is readily available; in addition, pneumothorax must be conceived as only a part of the collapse therapy program. The focusing of attention on details of management should also connote that, in the future, unfavorable results which can be attributed to misuse will be recognized as such and not allowed to furnish the basis for a reaction against its continued judicious use.

It should be mentioned now that all reference to pneumothorax in this discussion assumes that it is combined with bed rest. We believe there is agreement that, from a strictly medical standpoint, mass ambulatory pneumothorax is a makeshift. It is of value but only within its limitations; its justification must be primarily on public health and economic grounds.

INDICATIONS

Indications for pneumothorax have been the subject of a vast number of articles and are undoubtedly phases of pneumothorax about which there will never be any general agreement. The reason for this is the fact that individual physicians vary in the interpretation which they place in the effect of the various methods of treatment used to control tuberculosis. This is a natural trait and will always be present. However, our observation has been that, within reasonable limits, this phase of the subject is of relatively minor importance, and that, other than to avoid extremes, the matter of indications is of far less significance than a knowledge of contraindications and of the details involved in proper management once pneumothorax is induced. It is sufficient to state that unless there are specific contraindications, cavity with positive sputum and progressive disease remain the classic indication for pneumothorax. In deciding on this question in any individual case, the possible dangers, inconveniences, and expense must be balanced with the probable benefits and especially the individual need for these benefits. This leaves much room for clinical judgment which is as it should be. However, in considering the problem of pneumothorax it is well to remember that a truism, applicable to all branches of medicine, is that unnecessary surgical treatment is to be avoided—that, therefore, in general those cases which will recover without major collapse therapy should be allowed to do so. Advocacy of this course in no way detracts

from the great value of collapse therapy; it merely recognizes the acknowledged fact that many cases of tuberculosis will recover without it.

MAJOR FACTORS WHICH MAY CONSTITUTE CONTRAINDICATIONS TO ARTIFICIAL PNEUMOTHORAX

There are certain conditions under which pneumothorax may be definitely contraindicated either temporarily or permanently even though collapse therapy is indicated. This aspect we consider of major importance.

1. *Type of Disease.*—It is well known that exudative disease retains the greatest proportion of its original power to heal and contract and it is, therefore, in these cases that the maximum benefits of pneumothorax are obtained. However, all disease of this type does not require pneumothorax. On the other hand, it is becoming obvious that in patients with disease which is almost entirely fibrous, and particularly when it involves the greater part of one lung, pneumothorax is usually definitely contraindicated. In these cases effective collapse is rare since adhesions are frequently numerous. In addition, the diseased area has already undergone marked scarring with a resultant decrease in the size of the affected lung. Thus, even if a fairly free pneumothorax space is found, re-expansion often fails to occur; if it does take place, it is usually only by shift of the mediastinum, thus increasing the size of the contralateral lung which eventually means emphysema and further diminution of respiratory reserve. In the vast majority of such cases which require collapse therapy, thoracoplasty is the procedure of choice. The result is usually permanent, there is very low mortality and morbidity, and few late complications. In addition to these important factors there is not the stress placed on the opposite lung as described above, and in the future application of collapse therapy this factor must be taken into consideration more uniformly.

In acute pneumonic tuberculosis it is wiser to allow a few weeks or months of bed rest before inducing pneumothorax in order to lessen the chance of serious pleural infection and possibly, by educating the patient on correct posture and methods of raising sputum, also to lessen the chance of bronchogenic spread of disease. There is much less to fear from adhesions since the perfection of details of closed pneumonolysis. It is realized that there is a great difference of opinion on the advisability of immediate pneumothorax in this type of lesion. It is, however, common experience that results gained with immediate pneumothorax have generally been disappointing; in the Negro they have been almost universally so. Although results are relatively unsatisfactory under any regime, the most effective course seems to be a period of bed rest usually followed by pneumothorax.

2. *Special Conditions Which Constitute Indications for Primary Thoracoplasty Without Attempting Pneumothorax.*—It has been thought in the past that pneumothorax should always be tried before consider-

ing thoracoplasty. However, there are certain types of lesions which should be regarded as unsuitable for pneumothorax and in which primary thoracoplasty is the procedure of choice. This indicates that not only is it thought that pneumothorax will not effectively control the disease but that, in addition, it may be definitely harmful. This stand appears especially justified in view of the safety, permanence, and low rate of complications which the modern thoracoplasty can show. Primary thoracoplasty is indicated when permanent collapse is needed,* when the chances of serious pleural complications with pneumothorax are prohibitive, or when interference with bronchial drainage makes pneumothorax dangerous. The more specific indications are these:

(a) *Large Apical Cavity:* Under these circumstances, pneumothorax should seldom be attempted. Adhesions which are nearly always present may contain part of the blood supply to the cavity wall and cutting them will often cause slough of the wall with resultant bronchopleural fistula and fulminating empyema. This puts a grave added factor on the patient, one which may in itself be fatal. In addition, with the very large cavities and extensive destruction, eventual re-expansion, even when possible, is not pleasant to contemplate so that from a long-range viewpoint permanent surgical collapse seems much the better procedure. Some of these cavities are difficult to close completely by any means. If the surrounding disease appears very exudative and the patient is toxic, a preliminary period of bed rest before surgical intervention is advisable. Otherwise, thoracoplasty is done with a minimum of delay. This course is also safest when there is extensive excavation throughout one lung. Permanent collapse is then desired and a temporary procedure (pneumothorax) should not be used unless the location of the disease is such that the more concentric collapse obtainable by pneumothorax is absolutely necessary for its control.

(b) *Extensive Fibrous Disease:* This contraindication to pneumothorax has been discussed under the section Type of Disease. As stated there, permanent collapse is best for the reasons given, provided, of course, that collapse is indicated by the presence of a cavity. Many of these patients have a great amount of resistance and may live for years in comparatively good health. However, thoracoplasty is often indicated as a combined economic and public health measure so that rehabilitation may be effected with a greater degree of safety to the public and, by the same means, permanent costly hospitalization avoided.

(c) *Bronchostenosis:* In cases of pulmonary tuberculosis complicated by encircling and stenotic disease of the bronchus, pneumothorax is usually contraindicated. Patients with such complications are prone to frequent bouts of high fever as a result of thick secretions collecting near the stenosis. Bronchoscopic aspiration will frequently terminate these episodes abruptly. However, induction of pneumothorax is often

*This is in line with what should be a basic principle of phthisiotherapy: to produce permanent collapse only through a measure designed for permanent collapse. Churchill[5] has brought out clearly the importance of this principle.

sufficient to convert a partial occlusion into a complete occlusion. As a general rule, primary thoracoplasty is the therapeutic procedure of choice although eventual prognosis must be guarded with any form of treatment. At least, by following this course, there is not an infected pleural space with which to contend. Thoracoplasty is indicated not only for control of the parenchymal disease but also because it may lessen the chances of pulmonary suppuration in the field distal to the stenosis. In a very small number of these cases, particularly those which show little active parenchymal disease, pneumonectomy may be indicated.

(3) *Presence of Active Tracheobronchial Disease.*—In the past few years a tremendous amount of knowledge has been acquired in this field. It is now realized that the presence of this complication may alter materially both the prognosis and treatment of tuberculosis and that, therefore, every effort should be made to diagnose it before active treatment is begun.[6] The diagnosis of tracheobronchial tuberculosis finally must rest on bronchoscopic visualization. However, there are certain signs and symptoms so strongly suggestive that they furnish valuable indications for bronchoscopic examination. Chief among these are the following.

(a) Positive sputum without obvious source. In many cases in which the parenchymal disease appears to be controlled but in which the sputum remains positive, ulceration of the bronchus may be found.

(b) Cyanosis and dyspnea without apparent cause.

(c) Marked daily variations in character and amount of sputum.

(d) Symptoms which are out of proportion to the visible parenchymal disease.

(e) Dense, homogeneous shadow of lobar or lobular distribution indicating wet or dry atelectasis. In many of these, the so-called classical signs of atelectasis are absent and are not necessary for the diagnosis.

(f) So-called "hilar flare" type of shadow in which the shadow appears to flare out from the hilar region. Included in this group are also those cases showing the greatest concentration of parenchymal disease around the hilar region.

(g) Wheeze, subjective or objective, but in either event a finding of great importance. It frequently leads to bronchoscopic examination and every patient should be questioned as to its presence and should also be examined for objective evidence of it.

Ulceration of the bronchus having been found, the question of treatment of the parenchymal disease then arises. If the ulceration is small and superficial, a fairly short period of treatment with 30 per cent silver

nitrate is usually sufficient to produce healing. In this case it is moderately safe to overlook completely the healed ulcer, and to proceed with whatever treatment appears indicated for the parenchymal disease. Aspiration of secretions at the time of bronchoscopy helps to make this safer.

However, if there is deep extensive ulceration, or, as mentioned previously, bronchostenosis, extreme hesitance must be shown as to inducing pneumothorax. In the latter, it is nearly always definitely contraindicated; in the former, there should be a preliminary course of bronochoscopic treatments of the ulcer and aspiration of retained secretions. If pneumothorax then is absolutely indicated by the presence of cavity or uncontrolled disease in an area which is not accessible to permanent surgical collapse, it may be induced with the hope that the preliminary bronchoscopic treatments may have lessened the chances of complications. But also it should be realized that under these conditions serious complications are frequent and indications for pneumothorax must be stronger than usual. There is often disease in the submucosa even when the mucosa appears healed and complications as described under Bronchostenosis are fairly frequent. Unexpandable lung, with all of its implications, is probably the most serious late complications. In the earlier stages, atelectasis is frequent but much more serious is the occurrence of anaerobic infection with excavation distal to the stenosis. Occasionally, the presence of excavations out of all proportion to the amount of tuberculous disease, and occurring shortly after the induction of pneumothorax, is the first indication of tracheobronchial disease. Particularly is this so in those cases in which the affected lobe quickly becomes solid.

Thoracoplasty effectively controls the parenchymal disease in most of these patients and is accompanied by few of the dangers inherent in pneumothorax.[7]

MAJOR FACTORS INVOLVED IN IMPROVED MANAGEMENT OF ARTIFICIAL PNEUMOTHORAX

A knowledge of how to use pneumothorax once it is induced shares equal importance with a proper conception of contraindications in determining results of tuberculosis treatment. Mastery of all the details involved in proper management requires a broad understanding of tuberculosis and constant attention to individual factors uncovered in each case as the procedure progresses. These factors are of paramount importance and unless pneumothorax is administered or supervised by one familiar with them, it becomes a haphazard procedure of doubtful therapeutic value and one capable of producing serious complications.

The more important factors essential to proper management are as follows.

1. *Early Re-expansion of Ineffective Pneumothorax.*—It is impossible to put sufficient emphasis on this point and it should be regarded as

by far the most valuable single means of improving the results of tuberculosis treatment. Every physician doing work on tuberculosis can recall failures of this sort from the past, many of which had tragic end results. It seems that the importance of this is still not sufficiently recognized even among workers in the field, since there are often seen, even now, and in good sanatoriums, cases in which pneumothorax is continued long after it is obviously ineffective. The disastrous results of this may be twofold: Not only does the parenchymal disease remain uncontrolled, but also there are created conditions favorable for serious pleural complications. Thus, many months are wasted, and quite often during this time the patient's clinical condition has been made worse by pleural tuberculosis and by bronchogenic spread from the uncontrolled disease in the underlying lung.*

The decision as to the effectiveness of pneumothorax should be made, in the vast majority of cases, in a few days or weeks. Frequently, an expiration film taken after the third or fourth refill will give sufficient information to make this decision. Early re-expansion can be effected with a minimum of serious complications, and in this way continuation of the procedure will be limited to those patients in whom it is therapeutically effective. Those in whom pneumothorax could not be effectively administered will have the benefit of prompt surgical treatment if indicated. Thoracoplasty is now highly developed and relatively safe and will be given to these patients early, while they are in good condition, and will be necessary only for control of the parenchymal disease. If, however, they are subjected to a long period of ineffective pneumothorax, they are usually faced with the necessity of such operative procedure eventually, but only after months or years in a sanatorium and often at a time when their general condition has deteriorated because of pleural infection, amyloidosis, or bronchogenic spread of disease. Operation, then, must often be performed to obliterate an empyema cavity which is far more serious.

2. *Proper Conception and Use of Closed Pneumonolysis.*—Recent studies have emphasized the value of free pneumothorax spaces in de-

*Failure to recognize that pneumothorax is not invariably beneficial or neutral in action but often is definitely harmful (partly actively and partly passively by delaying surgical collapse) has been responsible for most of the statistical confusion regarding the measure and for the ill repute into which it has fallen in some quarters. Evidence of the manner in which this may arise is found in the report of Jennings, Mattill, and Nemec,[8] in which therapeutic results were correlated with the type of pneumothorax space; with a satisfactory space 4.2 per cent were dead, with a partly satisfactory space 30.6 per cent, with an unsatisfactory space 66.2 per cent, and with no space 42.8 per cent. Thus, the fatality rate was approximately 25 per cent higher in those with an unsatisfactory space than in those with no space; paradoxically, the finding of a pneumothorax space made prognosis worse. Since the patients with an unsatisfactory space totaled 44 per cent of all their cases, an undifferentiated statistical study of pneumothorax (which is what most statistical studies are) would have resulted only in the beneficial effects being diluted and, in part, counterbalanced by the harmful effects and would have furnished no information as to the real value of the measure in those patients in whom it was effective nor of the real potential of collapse therapy in the entire group.

The obvious solution to such a dilemma is universal acceptance and application of this policy; unless pneumothorax is effective or through pneumonolysis can rapidly be made so, it should be abandoned promptly and alternative measures applied. Until that policy becomes an inherent part of pneumothorax therapy, further mass statistical studies will tend only to compound confusion.

termining the end result of pneumothorax treatment.[8, 9] It is inconceivable that a proper collapse therapy program can be carried out without having the operation of closed pneumonolysis always available. The technique has been improved so much that serious complications are now rare. An adhesion, per se, is not considered to constitute an indication for the procedure, but if there appears to be any tension through the diseased area, it is believed that the safer course is to have the adhesions severed. A large percentage of pneumothorax patients in sanatoriums should now receive this aid and it is undoubtedly one of the most important of modern developments. It is probable that the frequent use of this accessory procedure will greatly improve the end results of pneumothorax as in many of the cases in the past the diseased area was shown suspended by adhesions in such a way that really complete relaxation of that portion of the lung was not possible. In such a way, many cavities were thought to be closed only to show up again when re-expansion was permitted some years later.

There is no more reason for considering programs of pneumothorax without pneumonolysis as modern pneumothorax than there is for considering Brauer or other outmoded types of thoracoplasty as modern thoracoplasty, for each is a halfway measure.

X-ray films may be grossly inaccurate in outlining pleural adhesions even though many positions are used. If there is any doubt as to the operability of a case, thoracoscopic examination should be performed since this gives a far more accurate visualization than does the x-ray film. It was formerly believed that several months must elapse before pneumonolysis could be done. Now, however, the operation is carried out as soon as there is sufficient space, and it is easier, technically, at this early period. In ascribing complications such as simple effusion and empyema to this operation, it should be remembered that it is usually performed in the first six months and that it is in that same period that the majority of such complications occur even without operation.

While the very great value of pneumonolysis must be emphasized, there are also some contraindications to its use. There is now rather general agreement that the incidence of serious complications varies in direct proportion to the extensiveness of the operation. Therefore, re-expansion followed by thoracoplasty is usually preferable to an extremely extensive pneumonolysis. Of course, under certain circumstances this increased risk will have to be assumed, and this applies particularly to patients with advanced disease in the contralateral lung. As a general rule, however, very extensive pneumonolysis is contraindicated in unilateral disease.

The other set of conditions under which pneumonolysis should not be used is a large, peripheral cavity suspended by heavy, dense, adhesions. In many such cases the cavity wall receives part of its blood supply through the adhesions, and severance of them may cause slough

of the wall with serious pleural infection. Again, under these circumstances, re-expansion followed by thoracoplasty is preferred unless the condition of the opposite lung is such as to necessitate assuming this extra hazard.

3. *The Proper Conception of the Mechanics of Pneumothorax.*—This indicates that, fundamentally, pneumothorax is to be regarded as a procedure of relaxation and not one of active compression. Real compression pneumothorax is rarely needed and may do a great amount of harm. By giving frequent, small refills and performing pneumonolysis early, the diseased lobe will be allowed to concentrate into a smaller and more relaxed area. It is only in this way that "selective collapse" may be hoped for. Even this will not assure it, but rapid reduction of lung volume will almost certainly ruin any chance of it and, in addition, may tear adhesions and cause pleural infection. Especially in the more acute type of disease in which pneumothorax is used, rapid collapse may be disastrous. Likewise, very marked reduction of lung volume is usually neither necessary nor desired. The unnecessary collapse of normal tissue is a most potent source of late complications of pneumothorax.

The increasingly frequent use of pneumonolysis has made it feasible to carry out pneumothorax in this desired manner much more uniformly. In the past, contraselective collapse due to adhesions often made it impossible.

4. *Re-expansion in Cases With "Tension Cavities."*—Frequently cases are seen in which even with the pneumothorax space anatomically perfect, cavities will remain stationary or even actually increase in size. In such cases they appear tense and assume a spherical shape, these being the so-called "tension cavities." The mechanism is commonly thought to be ball-valve effect at the cavitary bronchus allowing ingress but not egress of air. In this way, a positive pressure is built up within the cavity, and the pneumothorax seemingly serves only to aggravate the condition. In such circumstances it must be assumed that the pneumothorax is not only useless but actually harmful since many of these cavities promptly close with re-expansion. By recognizing this type of cavity and realizing the general ineffectiveness of pneumothorax in closing it, a useless pneumonolysis may also often be avoided. Cavernostomy may eventually become a real importance in these cases in which the bronchial factor predominates.

5. *Re-expansion of Effective Pneumothoraces When They Are Believed to Have Controlled the Disease Adequately.*—This is a problem that is admittedly hard to face, and the question of when to re-expand a pneumothorax often seems unanswerable. However, the present trend toward longer and longer pneumothoraces in all cases is not justified. It is believed that here again individualization is of utmost importance and that the amount of disease originally present, as well as several other factors, must be summed up in order to make the decision. But

it should be remembered that complications can occur at any stage of the procedure and, therefore, if the physician believes it has been therapeutically adequate, it should not be continued indefinitely simply because that is apparently the easiest immediate course to follow. Many cases of unexpandable lung result from the extremely long-continued pneumothoraces, and in many others there is "false re-expansion," which means that although the pleural space is obliterated, this has occurred only as a result of mediastinal shift. In certain instances this may have grave late consequences by producing emphysema of the contralateral lung with resulting respiratory distress.

By and large, the need for really prolonged pneumothorax is an indication of inadequate attention to choice of cases and the question does not often arise if the principle of primary thoracoplasty is accepted and carried through in patients with extensive tissue destruction, large thick-walled cavities and/or widespread fibrous disease.

MANAGEMENT OF COMPLICATIONS OF PNEUMOTHORAX

It is now widely realized that the successful treatment of pleural effusion or empyema requires intensive active efforts aimed at keeping the space as dry and as free of infection as possible.

We believe, however, that there is not sufficient recognition of the fact that cases showing either persistent clear fluid with symptoms or tuberculous empyema which does not clear promptly, represent potentially serious problems—problems which may constitute sufficient indications for prompt change of treatment. Not only may these factors cause severe, and at times rapid, deterioration of the patient's general condition but, through pleural thickening, they may predispose to ultimate difficulty in re-expanding the lung, thus being more insidious, but no less real, in their harmful effect. Under these circumstances the threat of the original parenchymal disease must be reappraised routinely so that a judicious decision may be made as to the justification for further continuation of the pneumothorax. In such cases, the availability of surgical collapse is to be kept in mind if re-expansion is done and the parenchymal disease proves to be uncontrolled. Reasoning along these lines, it may sometimes be found that in apparently controlled cavitative basal lesions, in other lesions which would require too extensive thoracoplasty or, in poor surgical risks, the continuation of pneumothorax, even though complicated by severe pleural infection, is justified. Under these circumstances, the increased danger is fully realized but is believed to be less than that of the uncontrolled pulmonary lesion which would probably appear with re-expansion.

On the other hand, in good-risk patients with unilateral disease confined to the upper part of the lung, these complications are almost always sufficient to indicate discontinuation of the pneumothorax, this to be followed by thoracoplasty if necessary. From a long-range viewpoint,

this course is usually much the safer one for the patient, and a long-range viewpoint is highly important under such circumstances.

It has been our experience that in the vast majority of cases, serious complications of pneumothorax can be ascribed to faulty choice of patients or to poor medical management; with meticulous attention to details, they become relatively uncommon. Tuberculous empyema, in particular, should no longer rate as a major problem.

The fact that most of the serious complications of pneumothorax are preventable is of fundamental importance and must receive more emphasis in the future. The factors involved in such prevention have been discussed under various headings. Briefly, however, they are:

(1) Early re-expansion of ineffective pneumothoraces.

(2) Recognition of certain definite contraindications to pneumothorax.

(3) Recognition of certain definite contraindications to pneumonolysis.

(4) Early, judicious use of pneumonolysis when not contraindicated.

MINIMUM STANDARDS FOR STATISTICAL STUDIES

The difficulty in obtaining really comparable controls complicates interpretation of statistical data in pneumothorax therapy. Nevertheless, this has not been the sole or even the major factor favoring the present state of confusion on the subject. Rather, this has arisen principally because there have been no standards to apply to cases going into such series. In other words, the term pneumothorax has been used as though it were strictly definitive whereas the measure itself has been used in ways anything but definitive. Thus, most statistical series comprise cases in which the term may mean anything or nothing. It may mean an effective pneumothorax or an ineffective pneumothorax; pneumothorax complemented by pneumonolysis when indicated or with no such aid; pneumothorax combined with adequate sanatorium care or largely ambulant. All these and other variations are included in mass studies and because there is this fundamental confusion as to what is being analyzed, conclusions cannot be anything but indefinite, vague, and, at times, misleading.

The logical remedy for this unsatisfactory situation would seem to be the establishment of certain minimum standards to be met by cases going into such series. The following are suggested as possible adequate standards which are still limited enough to be practicable:

1. Pneumothorax shall be combined with sanatorium care. Ambulatory pneumothorax must be recognized as a therapeutic makeshift from a strictly medical viewpoint.

2. Pneumonolysis shall be used as an integral part of the collapse therapy program.

3. Effective and ineffective pneumothorax shall be sharply differentiated and other measures substituted for the latter, which will then be considered an exploratory procedure, not therapeutic.

While these conditions are few in number, strict adherence to them represents the difference between a careful, logical, well-conceived program and one which may be haphazard, inexact, and capable of seriously complicating the whole course of tuberculous disease.

SUMMARY AND CONCLUSIONS

This discussion is offered in the belief that continued failure to establish and to emphasize adequate standards for artificial pneumothorax has constituted a fundamental defect of collapse therapy. For improved perspective now makes it clear that pneumothorax may act in widely different ways and that, as with most surgical procedures, therapeutic results are favorable only in proportion to the care exhibited in its use and to the faithfulness with which basic, objective principles are carried out. The corollary to this premise is that studies of a statistical nature which do not take into consideration the question of minimum standards are of little or no value in determining the actual potential of the measure.

I have outlined in as concise a form as possible the major points which, in our experience, have contributed toward a more rational understanding of pneumothorax. Some of these factors are the result of recent technical developments; most, however, merely represent the application of ordinary sound surgical principles. It seems probable that the widely divergent opinions as to the value of pneumothorax are mainly a reflection of the many illogical ways it has been used, that once the present loose conception of it is corrected and it comes to be used in such a way that the term pneumothorax automatically connotes an effective well-managed pneumothorax, then the controversy over its merit will largely disappear.

The application of collapse therapy along these general lines will result in a moderate percentage decrease in the use of artificial pneumothorax and a moderate to marked percentage increase in the use of thoracoplasty.

REFERENCES

1. Drolet, G. J.: Present Trend of Case Fatality Rates in Tuberculosis, Am. Rev. Tuberc. 37: 125, 1938.
2. Soderstrom, K. M.: Collapse Therapy in Moderately Advanced Tuberculosis, Am. Rev. Tuberc. 44: 173, 1941.
3. Drolet, G. J.: Collapse Therapy, Am. Rev. Tuberc. 47: 184, 1943.
4. Bentley, F. J.: Artificial Pneumothorax, Experience of the London County Council, Medical Research Council Special Report Series, No. 215, His Majesty's Stationery Office, 1936.
5. Churchill, E. D.: Discussion of Paper on Extrapleural Pneumothorax by Dolley, F. S., Jones, J. C., and Skillen, Jane, Am. Rev. Tuberc. 41: 403, 1940.
6. Rafferty, T. N., and Shields, D. O.: Management of Pulmonary Tuberculosis Complicated by Bronchial Tuberculosis, J. Thoracic Surg. 12: 225, 1943.
7. Chamberlain, J. M., and Gordon, J.: Treatment of Endobronchial Tuberculosis, J. Thoracic Surg. 11: 292, 1942.
8. Jennings, F. L., Mattill, P. M., and Nemec, F. C.: Artificial Pneumothorax, Am. Rev. Tuberc. 42: 431, 1940.
9. Hjaltested, O., and Törning, K.: Clinical Aspects of Pneumothorax Therapy, Brit. J. Tuberc. 33: 4, 1939.

AMBULATORY PNEUMOTHORAX[1, 2]

Some Interesting Experiences Encountered over a Period of Ten Years in a Teaching University Clinic

H. I. SPECTOR AND H. E. OPPENHEIMER

Much has been written about pneumothorax, but comparatively little is found in the literature about the results obtained with ambulatory pneumothorax treatments and still less regarding the medical and social complications arising during the course of ambulatory pneumothorax treatments.

It occurred to the writers that the experiences encountered and the results obtained in a University Teaching Clinic over a period of ten years, where different physicians have given the treatments to the same patients, might be of interest.

In order to shorten the stay of the pneumothorax patients at the University Sanatorium, Mt. St. Rose, an ambulatory pneumothorax clinic was opened at one of the St. Louis University hospitals on November 1, 1930, which is still in existence. This University pneumothorax clinic is one of the oldest clinics in this section of the country. During these ten years, cases referred for treatment were mainly from Mt. St. Rose, but patients from other sanatoria and hospitals were accepted for refill treatments. An initial pneumothorax was never attempted in this out-patient clinic because, though we believe that it may be justifiable for public health reasons, it is not an ideal way of starting pneumothorax treatments. Furthermore, we contend that, with few exceptions, it is too dangerous a procedure to try in an ambulatory clinic. In emergencies, patients were given the initial treatment in the hospital proper and then continued in the out-patient department.

Briefly, the general routine was as follows: Every new patient referred to us for treatment was given a complete examination in the chest clinic. The frequency of refills and the amount of air given was then decided upon. With a few exceptions, the principle of low tension pneumothorax was used for we maintain that this procedure is the safer one. All patients were kept at partial bed-rest at first; exercise was gradually increased until they were able to do part-time work. Patients were encouraged to go to the Occupational Work Shop for part-time work, since such type of follow-up therapy is very helpful in the economic rehabilitation of the patient (1, 2).

As has already been described in a previous publication by one of us (3), the duration of pneumothorax treatments depended somewhat on the type and character of the existing disease before pneumothorax was instituted. In brief, exudative unilateral disease was kept collapsed a shorter period, usually three years, while patients with previously caseo-pneumonic tuberculosis with or without cavitation were kept collapsed at least five years.

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[2] Read before the Faculty Seminar, St. Louis University, March 27, 1941.

Before permitting reëxpansion of a lung, certain requirements were necessary, such as freedom of symptoms, repeated negative sputa for at least a year, a normal Schilling count, stationary physical signs, a maintenance of weight and the ability to do either partial or full-time work.

Reëxpansion of a lung was accomplished in three ways, either by increasing the time interval between refills, decreasing the amounts at the regular intervals or both. As the lung reëxpanded and came close to the chest walls, roentgenograms were taken and together with the bacteriological and stethoscopic findings were studied for possible reopening of cavities or other evidence of active disease. In most reëxpanded cases a serous fluid developed because of the increase in the negative pressure. In some cases a shifting of the mediastinum to the pneumothorax side took place. In some instances relapses occurred, but it should be

TABLE 1

End-results of "reëxpanded cases"

Total number reëxpanded						21
By choice	17	Tuberculous	12	9 are well	7 years	1
					6 years	1
					5 years	4
					1 year	1
					2 years	1
					6 months	1
				2 relapsed in opposite lung		
				1 Recollapsed because of massive effusion on reëxpanded side—well and working three years		
		Nontuberculous	5	3 dead		
				2 living		
Obliterative	4	Well and working		5 years		1
				3 years		1
				2 years		2

remembered the patients served were in the very low economic bracket which might be the explanation in part for these relapses.

In addition to making it possible for an earlier discharge of patients from the University Sanatorium, Mt. St. Rose, this small clinic served to train twenty resident physicians in the principles and practices of pneumothorax treatments, each physician receiving six months training, and medical students, junior internes and nurses being the spectators.

The many interesting experiences and complications, physical and socio-economic, encountered during the ten-year period from November 1, 1930 to November 1, 1940, as well as the effectiveness of ambulant pneumothorax treatment from the viewpoint of rehabilitation follows:

This study covers 101 cases, all white, 5 of which were nontuberculous. There were 61 females and 40 males in age groups varying from fifteen to fifty-four, the majority (69 per cent) falling in the age group fifteen to twenty-nine. The tuberculous cases were both in the moderately advanced or far advanced group.

No minimal cases were included. Most of the cases had unilateral disease. In the group of 96 tuberculous patients there were 10 with bilateral disease, 8 of whom were given pneumoperitoneum refills and 2 bilateral pneumothorax treatments simultaneously.

TABLE 2

Complications during treatment

Medical

Spontaneous pneumothorax incidental to treatment	5	Mixed empyema........ 2	Died later........ 1
			Recovered........ 1
		Serous effusion with recovery	3
Pneumonia in opposite lung with recovery	1		
Acute appendicitis with recovery	2	(1 in bilateral pneumothorax case)	
Seasonal bronchial asthma developing during treatment	3		
Chancre of tonsil	1		
Atelectasis of uncollapsed lung with recovery	1		
Air embolus in seven months pregnant woman with recovery	1		
Broken needle	1		

Some mediastinal herniae and effusions were present when patients came to clinic—a few developed in the clinic during period of treatment

Social

Some engagements
Some broken engagements
Some marriages
Some divorces
Pregnancies.............................. 5 in 3 patients
- Twice in 2 patients during period of pneumothorax treatment
- Once in 1 patient—following reëxpansion—twins with no ill effects

TABLE 3

Comparison of major complications

	NUMBER OF PATIENTS	NUMBER OF TREATMENTS	AIR EMBOLI	RATIO OF AIR EMBOLI TO NUMBER OF REFILLS	DEATHS	EMPYEMA: Number	EMPYEMA: Ratio of empyma to number of refills	EMPYEMA: Dead	SPONTANEOUS PNEUMOTHORAX	PLEURAL SHOCK
St. Louis University Clinic	101	4,692	1	1 in 4,692	0	2 (1 in lung abscess)	1 in 2,346	1	5	0
Chicago Municipal Tuberculosis Clinic	2,366	83,245	28	1 in 2,973	8	25	1 in 2,349	12	3	1

A total of 4,692 treatments were given by twenty physicians, 186 of which were pneumoperitoneum refills. The greatest number of pneumothoraces given to a single patient with complete reëxpansion was 197 over a period of seventy-four months.

A total of fifty pneumothorax refills were given to five nontuberculous cases mainly to control haemorrhage resulting either from bronchiectasis, lung abscess, mediastinal cysts or lymphosarcoma. While the immediate objective of controlling haemorrhage was achieved, ultimately the treatments had to be discontinued because they were ineffective in controlling the disease.

The status of the 101 patients at the end of ten years was as follows: 38 were still under treatment in the clinic; 26 relapsed and were sent back to the sanatorium and of these, 12 died later; in 21 the lungs were reëxpanded; the condition of 13 was not known; and 3 were under the care of private physicians and apparently well. The end results of "reëxpanded cases" are seen in table 1.

As far as economic rehabilitation is concerned, 45 were working full time sometime during pneumothorax treatment, 9 part time, 39 were not working and 8 could not be classified.

The medical as well as the social complications that occurred during treatment as well as a comparison of the major complications with those of the Chicago Municipal Tuberculosis Clinic are seen in tables 2 and 3, respectively.

CONCLUSION

From data presented, it seems justifiable to state that pneumothorax refills in the ambulant patient are fairly safe and effective in pulmonary tuberculosis. The rather high percentage of spontaneous pneumothoraces incidental to the treatments is expected under the circumstances and needs no further explanation. The relapses that occurred in many instances can be explained on the social and economic basis, since many of the patients were financially assisted by the local social agencies.

Ambulatory pneumothorax clinics are worth while adjuncts to the teaching of tuberculosis to the medical students and resident staff of a university hospital.

The writers wish to acknowledge with thanks the coöperation given them in this work by Dr. G. O. Broun, Director, Out-Patient Department, Firmin Desloge Hospital, and by Sister M. Anita.

REFERENCES

(1) Spector, H. I.: In what way does occupational therapy assist in the recovery from tuberculosis, J. Occupational Therapy & Rehabilitation, 1936, *15*, 41.

(2) Spector, H. I.: Employment for the ex-tuberculous patient, Am. Hosp. A., 1935, *37*, 376.

(3) Spector, H. I.: When therapeutic pneumothorax for tuberculosis should be instituted and when it should be discontinued, J. Missouri State Med. Soc., January, 1937, p. 9.

(4) Tice, F., and Hruby, A.: Collapse therapy at the Chicago Municipal Tuberculosis Sanitorium, Bull. City of Chicago Municipal Tuberc. San., 15–16–17, Years 1935–1936, p. 114.

COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS[1,2]

Comparative Value of Different Procedures

L. W. THOMPSON AND ROBERT M. JANES

There has been a great deal of discussion whether artificial pneumothorax and other forms of collapse therapy actually accomplish the two main objectives in modern sanatorium treatment, namely, (*1*) the reduction of the treatment period, (*2*) the production of permanent cures.

It is proposed to present herewith some statistics, together with some observations, which seem to indicate that a proper selection of cases for the different forms of collapse therapy is an important factor in attaining the objectives above mentioned.

MORTALITY WITHOUT COLLAPSE

In 1933 Barnes (1) published a report on the prognosis of non-cavernous phthisis in 314 cases not given collapse; the average duration of treatment was 10.6 months and the patients were followed for a period of one to fourteen years. The death rate was: minimal, 15 per cent; moderately advanced, 31 per cent; far advanced, 66 per cent.

At the end of three years, 40 per cent of positive-sputum cases were dead and 15 per cent of negative-sputum cases; of those under twenty years of age forty-four died within three years.

The presence of cavities makes the prognosis much worse. McMahon and Kerper (2) in 1933 published their findings on 296 cavity cases and found that spontaneous healing occurred in 40 per cent of cavities under 2 cm. in diameter, 20 per cent of 3 cm. in diameter, 13 per cent of 4 cm. in diameter and 6 per cent of those over 4 cm. in diameter. Spontaneous healing of cavities occurred in only 17 per cent of patients under twenty-five years of age.

Simpson (3) in 1935 published the results of a follow up of 1,601 cases with X-ray evidence of cavity and found that 60 per cent were dead at the end of five years. It is to be noted that the majority of these cases had cavities 2 cm. or less in diameter. The fact that the cavities which Simpson studied were diagnosed by X-ray must be emphasized for, generally speaking, only 25 per cent of cavities exhibit cavernous breathing and 10 per cent of cavity cases show no abnormal physical signs whatever (Bendove (4)).

ARTIFICIAL PNEUMOTHORAX

Clinicians can cite pneumothorax cases who have done well and an equal number who have not. It has been our impression for some time that most

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[2] Read before the meeting of the Canadian Tuberculosis Association, Toronto, Canada, June, 1941.

of the unfavorable reputation that pneumothorax has acquired was due to the old custom of using it almost exclusively on advanced cases. In these cases pleural adhesions frequently prevented an efficient collapse of the diseased area.

These cases instead of getting selective collapse, got a contraselective collapse. There is no more certain method of producing tuberculous empyema than putting tension on tuberculous lung contained in adhesions. It should be emphasized that the tissue in adhesions is frequently under considerable tension in the presence of quite negative intrapleural pressure. It is our belief that a pneumothorax which cannot easily be made efficient by cutting the adhesions or supplementary phreniclasia should be abandoned at once and another form of collapse used. This belief is substantiated amply by a 1940 publication of Jennings, Mattill and Nemic (5) in a review of twenty years' experience with unilateral pneumothorax on 1,027 patients.

Results of pneumothorax—Jennings, Mattill and Nemic

	PER CENT WORKING	PER CENT ALIVE BUT NOT WORKING	PER CENT DEAD
Satisfactory pneumothorax	81.9	13.4	4.2
Partly satisfactory pneumothorax	56.8	12.6	30.6
Unsatisfactory pneumothorax	23.1	10.2	66.2
No free space, therefore no pneumothorax	38.8	18.4	42.8

Jennings, Mattill and Nemic give the following illuminating figures on the latter two groups of cases, who did not have a satisfactory pneumothorax: no further collapse—249 cases, 74.6 per cent dead at the end of three years; further collapse—346 cases, 28 per cent dead at the end of three years.

THORACOPLASTY

When pneumothorax is unsuccessful the usual operation of choice is thoracoplasty. Four hundred twenty-four thoracoplasty operations were done on 162 cases from 1933 to 1938 inclusive. The number of case-years is sufficient to give a reliable indication of the prognosis after thoracoplasty. The results are given in the following tabulation.

Results on 162 thoracoplasty cases at the Toronto Hospital completed two to eight years

	NUMBER	PER CENT
Working full time	38	60.5
Working part time	60	
Improved	27	16.7
Unimproved or worse	7	4.3
Early deaths	7	4.3
Late deaths	11	6.8
Not traced	12	7.4

*Effect of thoracoplasty on sputum**

Sputum positive before thoracoplasty		128
Died with positive sputum from operative side	5	21
Half of untraced group	6	
Living with positive sputum from operative side	10	
Sputum conversion		83.5 per cent

* Definition of negative sputum: (*a*) patient reports no sputum; (*b*) 8 negative concentrated smears.

Gastric lavages and cultures were not used on this group of patients.

Thoracoplasty cases grouped according to condition before operation

	FAVOURABLE CASES (62 PER CENT OF TOTAL)	UNFAVOURABLE CASES (38 PER CENT OF TOTAL)
	per cent	*per cent*
Working full time	28.2	13.0
Working part time	47.4	21.0
Improved	16.0	27.5
Worse	4.2	12.3
Early deaths	0.8	12.3
Late deaths	0.8	11.0
Untraced	2.5	2.6

Discussion of Thoracoplasty Results

Four of the 7 early deaths were due to pulmonary embolism. Five of the 11 late deaths were caused by nontuberculous disease. The operative mortality in emypema cases was 25 per cent, compared to 3 per cent for the pulmonary cases. All but one of the empyema cases that died were secondarily infected before operation.

This experience has led us to treat all tuberculous empyemata by aspiration and irrigation with 1:3300 Azochloramid; 2 to 15 cc. of 1:500 Azochloramid are instilled at the end of the irrigation. This routine cures many tuberculous empyemata and prevents secondary infection in the others but it is quite time consuming.

Caseous type disease: Thirty-five per cent of the parenchymal cases showed no evidence of fibrosis and were classified as exudative-caseous type disease. The 6 late deaths from pulmonary tuberculosis occurred in this group; 8 of the 10 living cases with positive sputum from the operative side fall into this classification; 4 of these cases had a temporarily negative sputum. A very complete collapse of the diseased area must be produced in this type if subsequent liquefaction and evacuation of the caseous material, with the production of new cavities, is to be prevented. The other 4 non-fibrotic cases who have persistently positive sputum had thin-walled cavities surrounded by comparatively healthy lung. In our experience these thin-walled cavities surrounded by healthy lung are easier to collapse by extrapleural pneumonolysis than by thoracoplasty.

Indications for anterior stage thoracoplasty: It is easier to remove the anterior part of the first and second ribs and their cartilages from the back, when a

large curved incision is used for the upper posterior stage, than to remove them through an anterior incision. Unfortunately this has one distinct disadvantage, namely that the pectoralis minor is not divided when the ribs are completely removed from the posterior approach. In 5 of the above mentioned non-fibrotic cases with persisting positive sputum the pull of the pectoralis minor on the anterior part of the second, third and fourth ribs seemed to be the factor which prevented an efficient collapse. In 3 others, failure to realize the necessity to remove the transverse processes resulted in an inefficient collapse. When dealing with non-fibrotic upper lobe cavities, especially thin-walled ones, it is our present practice to include an anterior stage with division of the pectoralis minor in the plan of collapse.

The use of the Semb apicolysis: A limited apicolysis after the manner described by Semb is indicated in the treatment of thin-walled cavities near the apex surrounded by a good deal of healthy lung. A single stage thoracoplasty with apicolysis is useful for collapsing small apical cavities while in the process of active fibrotic contraction. Otherwise the Semb procedure would seem to be contraindicated because the cavity drops necessitating removal of more ribs.

Effect of disease in the contralateral lung: Forty-eight cases, or 28 per cent, had minimal or more disease in the opposite lung, by X-ray appearance not judged to be healed before thoracoplasty. Four of these died of this disease from one to five years after the operation. In 10 cases the disease in the opposite lung is worse producing positive sputum in 8 of them. If the disease in the better lung does not seem to be healed it is apparent that a pneumothorax should be started before thoracoplasty is done on the worse side. Fifteen cases with pneumothorax on the opposite lung have had thoracoplasties to June 1, 1941. Only one has died.

Effect of age and duration of disease on mortality: Seven cases, 30 per cent, of the age group above forty years (24 cases) have died whereas only seven per cent in the age group twenty to forty years. Patients who have had tuberculosis for more than five years and are more than forty years of age are particularly bad risks.

Right side compared to left side: There was no appreciable difference in mortality or conversion of sputum between right and left sided cases. Patients who have had a right thoracoplasty have, on the average, more dyspnoea.

Vital capacity: One-third of the cases had a vital capacity below 50 per cent of their normal average. The mortality in this group was twice as high as the group with vital capacity more than 50 per cent of their normal average.

EXTRAPLEURAL PNEUMONOLYSIS

Eleven patients had extrapleural pneumonolysis at the Toronto Hospital for Consumptives, Weston, prior to July, 1938. The results in these cases were disappointing because unsuitable cases were operated on and the operative technique and after-care left much to be desired. Therefore, a preliminary re-

port of the cases done since that period will give a better picture of the results that may be obtained

Extrapleural Pneumothoraces, July, 1938 to December, 1940

Total patients: 30 (2 had bilateral operations)
Right side: 14 operations
Left side: 18 operations

Patients were divided into predominantly exudative type, chronic caseous type and acute caseous pneumonic type.

Chronic caseous type—22 cases: Average duration of disease was 3.3 years. Westergren sedimentation rate varied from 10 to 45. Mean sedimentation rate was 22. Conversion of sputum was obtained in 18 of 19 cases who had positive sputum before operation (94.7 per cent). Closure of cavity according to x-ray evidence occurred in 17 out of 19 cases. Tuberculous empyema developed in 5 cases; 4 of these have been cured by aspiration and irrigation. Obliterative pleuritis developed in 3 cases but the sputum remains negative in 2 of these. One male, age fourteen, died one month after operation from peritonitis subsequent to rupture of a tuberculous ulcer; one female, thirty-two years of age, died ten months after her operation from bilateral renal tuberculosis.

Exudative type—4 cases: Average duration of disease was 5.5 months. Westergren sedimentation rate varied from 27 to 60. Conversion of sputum occurred in all 4. Closure of cavity, as seen by X-ray, occurred in all 4. Tuberculous empyema developed in 2 cases; both were cured. Both empyema cases had moderate tuberculous enteritis, now much improved by calcium and diet. None died.

Acute caseous pneumonic type—4 cases: Average duration of symptoms was 5.5 months. Westergren sedimentation rate varied from 70 to 77. Cavity closed in only one case, who later developed a bronchopleural fistula and empyema. All 4 cases died from pulmonary tuberculosis one month to one year

Preliminary report of 32 extrapleural pneumothoraces on 30 patients including 2 bilaterals

	CHRONIC CASEOUS	EXUDATIVE	PNEUMONIC PHTHISIS
Number of operations	22	4	4
Average duration of disease	3.3 years	5.5 months	5.5 months
Erythrocyte sedimentation rate (W)	10–45 mm. (mean 22 mm.)	27–60 mm.	70–77 mm.
Closure of cavity according to X-ray	86 per cent	100 per cent	25 per cent
Sputum converted	94.7 per cent	100 per cent	0
Tuberculous empyema			
Developed	5 cases	2 cases	1
Cured	4 cases	2 cases	0
Obliterative pleuritis	3 cases	0	0
Deaths	2 cases (nonpulmonary)	0	4

after operation. All had advanced tuberculous enteritis. Three cases did not develop tuberculous empyema until they became moribund.

Discussion of Results of Extrapleural Pneumonolysis

The most frequent complication following extrapleural pneumonolysis is tuberculous empyema in the extrapleural space. The more difficult the stripping of the pleura the greater the possibility of subsequent empyema. Apparently stretching the diseased lung tends to produce tuberculous empyema as in intrapleural pneumothoraces. The stripping should therefore be carried well down on the chest wall and mediastinum. The cases which developed obliterative pleuritis were those in which sufficient stripping had not been carried out. To obtain a good result the lung should be freed for at least two interspaces below the lower level of the pulmonary cavity, shown in the preoperative X-ray film. It is possible, then, to collapse the lung slowly by a gradually increasing positive pressure, reaching a maximum of 20 cm. of water at the end of one month. The air pressures used must be governed by frequent fluoroscopic examinations. After the first week it is better to keep the space dry and give nitrogen refills to those cases who continue to form fluid. Even clear fluid should be aspirated and Azochloramid instilled. Care should be taken not to injure the underlying lung with the needle. Patients with symptoms of tuberculous enteritis seemed more prone to the development of empyema.

One case developed staphylococcus empyema ten days after the operation. It was cured by daily Dettol irrigations and instillations. To-day such a patient would be given sulphathiazole.

CONCLUSIONS

1. Collapse therapy offers a much better prognosis for pulmonary tuberculosis than bed-rest alone. This is especially true for patients with cavities.
2. A satisfactory artificial pneumothorax is the treatment of choice but an inefficient pneumothorax is likely to be a liability rather than an asset.
3. Where an efficient pneumothorax cannot be established it should be abandoned at once and another form of collapse instituted.
4. If pneumothorax cannot be used thoracoplasty is the next safest and most widely applicable form of collapse therapy.
5. If a good anterior collapse from thoracoplasty is desired the pectoralis minor muscle should be divided.
6. Extrapleural pneumothorax is the treatment of choice for acute or chronic thin-walled cavities of 3 cm. in diameter or less which are surrounded by comparatively healthy lung. This is especially true of cavities in the apex of the lower lobes and lingual process of the upper lobes.
7. Extrapleural pneumothorax is the treatment of choice in adolescents with minimal lesions that progress or are stationary under bed-rest alone.
8. Extrapleural pneumothorax is often the treatment of choice where thoracoplasty is difficult or dangerous on account of bilateral disease, advanced non-

pulmonary tuberculosis or nontuberculous disease. Extrapleural pneumothorax is of little or no value in acute caseous pneumonic phthisis.

9. Cavities larger than 3 cm. in diameter which are surrounded by caseous disease are best treated by thoracoplasty.

REFERENCES

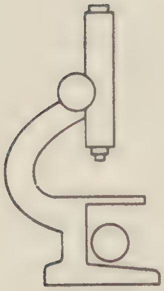
(1) Barnes, H. L.: The prognosis of noncavernous tuberculosis, Am. Rev. Tuberc., 1933, *28*, 660.

(2) McMahon, B. T., and Kerper, E. H.: The healing of tuberculous cavities, Am. J. M. Sc., 1933, *186*, 170.

(3) Simpson, S. E.: Cavities in pulmonary tuberculosis, Am. Rev. Tuberc., 1935, *31*, 658.

(4) Bendove, R. A.: The variable auscultatory signs of pulmonary cavities, Am. J. M. Sc., 1935, *190*, 60.

(5) Jennings, F. L., Mattill, P. M., and Nemic, F. C.: Artificial pneumothorax, Am. Rev. Tuberc., 1940, *42*, 431.



THORACOSCOPY IN PULMONARY TUBERCULOSIS

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INTRODUCTORY STATEMENT

THIS study was stimulated by a remark from a fellow physician in the course of a staff conference at the Olive View Sanatorium. The gist of the remark was that inasmuch as thoracoscopy was essentially a surgical procedure, it was not indicated in therapeutic pneumothorax in which pneumonolysis was apparently not feasible judging by the appearance of the adhesions in the roentgenograms.

As pointed out by many workers[1-5, 7, 8, 10, 12-14] and recently stressed by John C. Jones,[6] the only reliable method of determining feasibility of closed pneumonolysis is inspection of the adhesions in the course of thoracoscopy; roentgenography, though very helpful, is not without its limitations. Employing this concept as a starting point for further reasoning, it would seem inadequate therapy not to give the patient the benefit of thoracoscopy in instances in which pneumonolysis does not seem to be entirely out of the question by reason of diffuse adherence, provided it can be demonstrated that as a surgical procedure thoracoscopy is free of serious accidents and complications.

In order to determine how safe thoracoscopy was, the records of all patients subjected to thoracoscopy without pneumonolysis at Olive View Sanatorium were reviewed, paying particular attention to the type of complication and its time relation to the operation. The period covered extended from 1930 to September, 1942.

Thoracoscopy alone, without pneumonolysis, should not be credited with complications arising as a result of postoperative ''pushing'' of the collapse by excessively large refills in the attempt to convert adhesions not feasible for pneumonolysis into feasible ones; this is particularly essential because this series of patients consisted of mechanically unsatisfactory pneumothoraxes, a group especially susceptible to complications.

Regardless of the conclusions derived from this study relative to the safety of thoracoscopy it is admitted that, if patients with adhesions of roentgenologically doubtful feasibility are subjected to thoracoscopy, the procedure does become dangerous in the hands of the easily tempted operator for no other reason than that a larger number of difficult pneumonolyses is bound to be done and followed by a greater incidence of serious complications. On the other hand, thoracoscopy in the case

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of adhesions not feasible for pneumonolysis brings forth in an impressive way the ineffectiveness of the collapse and the danger and futility of maintaining it and thus often helps to bring about earlier abandonment of the ineffective collapse and substitution of an effective procedure.

PREOPERATIVE STATUS

This series consists of 73 tuberculous patients with mechanically unsatisfactory pneumothorax most of whom had sputum positive for tubercle bacilli and x-ray evidence of cavitation in the homolateral lung.

The type of infiltration in the homolateral lung was as follows: exudative in 42 patients, fibrotic in 1, and mixed exudative and fibrotic in 30. All but one were afebrile at the time of thoracoscopy.

The interval between the date of induction of pneumothorax and the date of thoracoscopy ranged from 1 to 32 months, and averaged 9 months. In 22 patients the interval was less than 6 months and in 49 less than 10 months. In 17 patients the interval was from 10 to 20 months and in 7 patients, 20 months and over.

Homolateral obliterative pleuritis with positive intrapleural pressures was present in 14 patients, 6 of whom also had a pleural effusion.

Homolateral pleural effusion existed in 15 patients, 6 of whom also had obliterative pleuritis, and was serous in 14 and purulent in 1. Of the 14 serous effusions, 9 were afebrile in onset and the remaining 5 had a febrile onset. Bacteriologic studies revealed that in the 9 cases in which the fluid was examined it was found to be negative for pyogens on culture. In 5 of the 9 cases examined the fluid was negative and in the remaining 4 positive for tubercle bacilli on culture; in only 1 was it also positive on smear. Of the 4 positive for tubercle bacilli the onset of effusion was febrile in 3; of the 5 negative for tubercle bacilli the onset was febrile only in 1.

OPERATION

The 73 thoracoscopies were done by five successive operators; I did only the last four during the year ending in September, 1942. Of this series, 5 patients were subjected to closed pneumonolysis some time prior to thoracoscopy and 3 other patients some time following thoracoscopy.

The duration of the operation ranged from 10 to 180 minutes and averaged 32 minutes for the 65 procedures for which this was recorded. The operation lasted 30 minutes or less in 43 cases, 60 minutes or less in the case of 59 patients, and over 60 minutes in 6 patients. These 6 prolonged procedures were done in the early 1930's and although the reason for it is not entirely clear in every case, technical difficulties with the thoracoscope accounted for prolongation of the operation. Pneumonolysis was not feasible in the case of all but 2 patients, and in these the procedure was limited to thoracoscopy because of severe dyspnea in one case and a cardiorespiratory reaction to locally injected novocain in the other.

The postoperative stay of these patients at the Sanatorium ranged from 2 weeks to 37 months and averaged 15 months. Eighteen patients stayed less than 6 months, 29 patients less than 10 months, 20 patients between 10 and 20 months, and 24 patients stayed 20 months or more.

Mortality attributable to thoracoscopy was zero. In the patients who died at the Sanatorium, death was due in 3 cases, 12 to 18 months postoperatively, to progressing pulmonary and/or intestinal tuberculosis, and in 1 case to a cerebral accident 4 months postoperatively. In 3 of these 4 patients the postoperative course was entirely uneventful and the remaining patient developed a persistent serous effusion 10 months postoperatively and died 4 months later of progressing pulmonary tuberculosis.

Morbidity following thoracoscopy will be discussed under the headings of hemorrhage, fever, spontaneous pneumothorax and bronchopleural fistula, pleural effusion, obliterative pleuritis, and extension of the pulmonary process, which is the approximate chronologic order in which accidents and complications of intrapleural operations occur.

Only 3 instances of hemorrhage could be found and all were slight; 1 was from the trocar wound externally and was described as due to failure to find the pleural space, and the remaining 2 were discovered in the course of postoperative aspiration of pleural fluid.

A temperature of 100° F. or over was arbitrarily chosen in this study to designate fever. Accordingly, 22 patients, or 30 per cent, were febrile. A maximum temperature of 100° F. was observed in 13 patients, 101° in 6, 102° in 1, and 104° in 2 patients. The duration of continuous fever ranged from 1 day to 20 weeks, an average of 2¼ weeks. The interval between thoracoscopy and the onset of fever was 0 in 19 cases, and 3, 6, and 44 weeks respectively, in the remaining 3 cases. All 3 patients developed a pleural effusion simultaneously with the onset of fever and all 3 received refills now regarded as too large; it is highly probable that thoracoscopy cannot be regarded responsible for these "late" complications.

Homolateral, serous, pleural effusion developed in 9 patients and persisted in 3 others who had it preoperatively as well. In 3 of the former it was transient and occurred within the first postoperative month, whereas in the remaining 6 it occurred in from 1½ to 10 months and persisted, eventually becoming purulent in 4 of these patients. On culture, tubercle bacilli were demonstrated in 1 of the 2 transient effusions and in all of the 6 persistent ones, 4 of the latter also containing tubercle bacilli demonstrable on smear as well. It will be noted that in 7 of the 15 patients with a preoperative effusion, thoracoscopy was followed by disappearance of the fluid.

All postoperative effusions with the exception of 2 purulent ones were negative for pyogens on culture, and the latter 2 were examined by smear only and were negative.

Spontaneous pneumothorax occurred in 3 cases in from 6 to 16 weeks postoperatively and was probably due to rupture of adhesions by refills of 500 to 600 c.c., currently regarded as heroic, in the effort to stretch the adhesions. A bronchopleural fistula developed in 1 case 3 days postoperatively; in this case the operation lasted over 2 hours and although it would seem that it was confined to inspection of adhesions, the record is not entirely clear on this point; moreover, 2 months earlier this patient was subjected to a closed pneumonolysis.

Obliterative pleuritis occurred in 8 of the 59 patients free of this complication preoperatively. Two of these left within 2 months and 1 had an open pneumonolysis 2 weeks following thoracoscopy; in 6 others pneumothorax was immediately discontinued. This left 50 patients with maintained collapse, 8 of whom developed obliterative pleuritis 6 to 40 weeks postoperatively.

The subject of extension of pulmonary disease cannot be discussed in the case of 15 patients either because they left the Sanatorium within 2 months postoperatively and were not x-rayed, or because pneumothorax was discontinued immediately. Of the remaining 58 patients, 5 showed definite contralateral extension of disease in from 1 to 10 months postoperatively; in 2 of these it was preceded by spontaneous pneumothorax or bronchopleural fistula and empyema.

RELATION OF OPERATION TO POSTOPERATIVE COMPLICATIONS AND DEVELOPMENTS

Fever.—The incidence of postoperative fever was found to bear practically no relationship to the length of the interval between thoracoscopy and induction of pneumothorax or to the presence of preoperative obliterative pleuritis. However, the type of infiltration in the homolateral lung and the duration of operation unquestionably influenced the incidence of postoperative fever; the latter was twice as great in those with exudative lesions as in those with mixed infiltration and two and one-half times as great in operations lasting over 60 minutes as in those lasting 30 minutes or less. It was rather surprising to find that postoperative fever was two and one-half times as frequent among those free of preoperative homolateral effusion as in those with one.

In 87 per cent of patients with postoperative fever its onset was immediately following thoracoscopy; it must be conceded, therefore, that postoperative fever was definitely due to the operative procedure. However, it is obviously not a serious sequel for the simple reason that the incidence of immediate fever of 102° F. and over, in the entire series, was only about 3 per cent.

Pleural Effusion.—The incidence of postoperative homolateral serous effusion showed the same relation to the type of homolateral infiltration and to the duration of pneumothorax as was observed in the case of fever. Among the patients with preoperative obliterative pleuritis the incidence of postoperative pleural effusion was three times as great as

among those without it. No relation was apparent between the incidence of postoperative effusion and the length of the operation.

The 6 postoperative effusions which appeared in from 1½ to 10 months postoperatively and which persisted cannot justifiably be regarded as due to thoracoscopy because of the length of interval and because of accompanying complications pointing to the presence of other factors such as "pushing" mechanically ineffective pneumothoraxes and subsequent rupture of adhesions. The 3 postoperative effusions which appeared within the first month and which were transient and unaccompanied by any complications were probably due to thoracoscopy. Among the 52 patients observed for two months and over postoperatively, free of serous fluid preoperatively and in whom pneumothorax was not discontinued, the incidence of postoperative effusion was only 17 per cent as compared to 20 per cent incidence preoperatively, which suggests that thoracoscopy did not contribute appreciably, if at all, to the incidence of this complication of pneumothorax.

Spontaneous pneumothorax, bronchopleural fistula, purulent pleural effusions and extension of pulmonary disease can be best considered together because of their associated pathogenesis in 5 out of the 7 patients falling into this group of postoperative developments. The fact that in most of these patients these complications occurred many weeks to a year postoperatively, the excessively large refills of air in those in whom spontaneous pneumothorax occurred and finally the 10 per cent incidence of these developments probably not exceeding the frequency with which they are encountered in similarly managed cases not subjected to thoracoscopy suggest that in this series thoracoscopy was not responsible for these complications. The reason for the recently reported incidence of bronchopleural fistula and empyema within 1 month following thoracoscopy alone, at the Sea View Hospital, is not understandable.[9, 11]

That *mixed infection* tuberculous empyema did not occur in this series lends weight to John C. Jones' statement that the usual source of pyogenic infection of the pleural space following intrapleural operations is traumatized lung rather than a "break in technique."[6]

Obliterative pleuritis postoperatively did not appear to bear any relation to the type of infiltration, duration of operation, etc. Among patients free of this condition preoperatively and observed for 2 months or over postoperatively the incidence of obliterative pleuritis was 16 per cent with an onset of 6 to 40 weeks postoperatively. It is stated that the incidence of obliterative pleuritis following closed pneumonolysis is definitely higher than in pneumothorax patients not subjected to the operation.[6] In this series where no division of adhesions was attempted the incidence of postoperative obliterative pleuritis was only 16 per cent as compared to an incidence of 20 per cent preoperatively, which suggests that thoracoscopy did not contribute appreciably, if at all to the incidence of this complication.

Obliterative pleuritis with eventual loss of the pleural space following thoracoscopy of a patient with inoperable adhesions and ineffective pneumothorax may be regarded as a physiologic, and incidentally desirable, development or end-result of ineffective collapse by pneumothorax. In many instances it is undoubtedly a fortunate development terminating an ineffective procedure subject to serious complications such as spontaneous pneumothorax, bronchopleural fistula, or pyopneumothorax with loss of function of the entire lung including uninvolved parts, and homolateral and contralateral extension of disease.

SUMMARY AND CONCLUSIONS

The preoperative status, complications and developments following 73 thoracoscopies done by 5 successive operators at Olive View Sanatorium over a period of about 13 years are presented. Of all postoperative complications and developments observed, it appears that fever was the only one directly attributable to thoracoscopy and that pleural effusion and obliterative pleuritis could possibly be classified as true complications if it were not for the fact that their postoperative incidence, over a longer period of observation, was even lower than the preoperative incidence. Even if regarded as true complications, their incidence was not high so that it must be conceded that thoracoscopy, though a surgical procedure, was free of serious accidents and complications in this series. The limitations of roentgenography in studying pleural effusions, despite its definite usefulness in most cases, has already been pointed out.

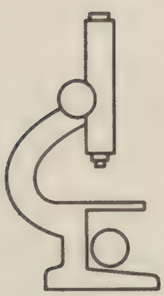
Once it has been demonstrated that thoracoscopy is safe and not replaceable by roentgenography, the obvious conclusion is that thoracoscopy deserves a wider application in order to render ineffective collapse effective where pneumonolysis is feasible and to discontinue pneumothorax at an earlier date and substitute an effective procedure, where pneumonolysis is not feasible, before disastrous complications of ineffective pneumothorax supervene.

The clerical assistance of, the Record Office staff of the Olive View Sanatorium is hereby gratefully acknowledged.

REFERENCES

1. Forsee, James H.: Closed Intrapleural Pneumonolysis in the Artificial Pneumothorax Treatment of Pulmonary Tuberculosis, J. Thoracic Surg. 2: 270, 1933.
2. Forsee, James H.: The Partial Cauterization of Pleural Adhesions by Closed Intrapleural Pneumonolysis, Am. Rev. Tuberc. 30: 287, 1934.
3. Head, Jerome R.: Thoracoscopic Pneumonolysis, Am. Rev. Tuberc. 20: 692, 1929.
4. Jeanneret, R., and Billiard, A.: Note sur la Pleuroscopie et les Sections D'adherences, Schweiz. med. Wchnschr. 72: 156, 1942 (Abstracted in Am. Rev. Tuberc. 46: 54, 1942).
5. Jones, H. A.: Closed Intrapleural Pneumonolysis, Am. Rev. Tuberc. 40: 722, 1936.
6. Jones, John C.: Surgical Aspects of Pleural Adhesions, California & West. Med. (Tuberculosis Supplement) 57: 29, 1942.

7. Matson, Ralph C.: The Cauterization of Adhesions in Artificial Pneumothorax by the Jacobaeus-Unverricht Method of Closed Pneumonolysis, Am. Rev. Tuberc. **19**: 233, 1929.
8. Newton, Harlan F.: Intrapleural Pneumonolysis, Am. Rev. Tuberc. **41**: 22, 1940.
9. Palitz, Leo, and Herman, Myron: Treatment of Tuberculous and Mixed Infection Empyema With New Irrigating Solutions, Quart. Bull., Sea View Hosp. **6**: 181, 1941.
10. Peters, Leroy S., and Cornish, P. G.: Results in Intrapleural Pneumonolysis, Am. Rev. Tuberc. **33**: 44, 1936.
11. Petroff, S. A., Herman, Myron, and Palitz, Leo: Treatment of Empyema, Am. Rev. Tuberc. **44**: 738, 1941.
12. Scarborough, C. Gerald: Thoracoscopy, Am. Rev. Tuberc. **40**: 389, 1939.
13. Smart, Joseph: Thoracoscopy and Adhesion Section With Special References to Indications and Results, Tubercle **21**: 81, 1939.
14. Welles, Edward S.: The Results of Cautery Pneumonolysis of Adhesions Complicating Artificial Pneumothorax, J. Thoracic Surg. **1**: 601, 1932.



RESULTS OF THORACOPLASTY[1]

A SYMPOSIUM PRESENTED AT THE TWENTY-FOURTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY, TORONTO, CANADA, JUNE 9, 1941

Surgery in Pulmonary Tuberculosis

RALPH ADAMS AND PAUL DUFAULT

A thirteen-year period of surgical therapy for pulmonary tuberculosis at one sanatorium is reviewed and the statistical results are reported. The material embraces 241 patients treated by thoracoplasty and 19 treated by extrapleural pneumothorax.

The important factors which have raised the rate of sputum conversion to 81 per cent in all sanatorium patients and 65.2 per cent following thoracoplasty and given an all-inclusive death rate of 15.7 per cent are analyzed. The discussion includes preoperative preparation, the use of ether as the anaesthetic agent, the type and technique of operation, the influence of apicolysis upon percentage and speed of conversion, postoperative care and complications, the reasons for failure and the causes of death in 260 consecutive cases.

Thoracoplasty

Late Results

GEORGE F. SKINNER, LACHLAN MACPHERSON AND IRENE ALLEN

The authors report 226 cases of thoracoplasty done between 1924 and 1940, more than half the total number having been operated upon since 1935.

Tables showing follow-ups at different periods with comparative figures are included.

Results with more extensive but more selective types of surgery as done in recent years are compared with those operated on five, ten and fifteen years ago.

The satisfactory cases are classified as apparently cured or improved. In

[1] The complete papers have been published in the Journal of Thoracic Surgery, October, 1941. The abstracts and summaries presented here are published by courtesy of the Editor of the Journal of Thoracic Surgery, Dr. Evarts A. Graham, and by courtesy of the publisher, The C. V. Mosby Company. The coöperation of the authors of these papers is gratefully acknowledged. [Ed.]

the former, cavities must be closed, sputum must be negative for tubercle bacilli and patients must be working. The improved patients are sputum-negative but either not sufficient time has elapsed to place them in the better group or some condition other than pulmonary tuberculosis has prevented them from working. All others are considered unsatisfactory or dead, there being only one case not traced.

The 226 cases are divided into three series The first 50, done between 1924 and 1932, with resection of small segments of eleven ribs and averaging over ten years since operation, show 58 per cent good results (apparently cured and improved) with an early death rate of 12 per cent and 16 per cent late deaths from tuberculosis; 10 per cent died of causes other than tuberculosis and 4 per cent were still living but unsatisfactory.

The second series of 50 cases, with total removal of the upper ribs and a more selective collapse, showed over 65 per cent good results five to eight years after operation and an early death rate of 4 per cent. There were 18 per cent late deaths from tuberculosis and 10 per cent were unsatisfactory.

In the third series consisting of 126 cases done since 1936 and including 90 thoracoplasties combined with apicolysis, there were 80 per cent good results and an early death rate of 3.2 per cent.

The figures for the three series at a comparable early period after completion were: apparently cured and improved, 66 per cent, 76 per cent and 80 per cent respectively.

Attention is drawn to a decline in the immediate good results three to five years after completion, while after this period figures remain more or less stationary. The late deaths from tuberculosis and the unsatisfactory cases were practically all in the poor risk group or those complicated by empyema.

The 4 deaths in the last series are discussed and it is pointed out that the addition of apicolysis did not increase the operative risk; results were better and complications less, when compared with the whole series.

This trend toward removing fewer ribs has been further augmented during the last year by Leahy's suggestion of inserting the scapula inside the sixth rib. This tendency toward a selective collapse may be carried too far, but with equally good results the appearance of the chest does count as well as saving of vital capacity.

The disadvantage in the apicolysis procedure is the dropping of the apical cavities to a less collapsible position in the hilar region. This is probably a real danger if an extreme relaxation is done routinely, but this danger would seem to be eliminated if the pneumonolysis is mostly in the region of the anterior mediastinum and the paravertebral gutter, leaving the lung attached at the very apex or allowing the apex to drop only a few inches. Relaxation in all directions, rather than extreme dropping of the apex, is the aim.

Analysis of 100 Consecutive Cases of Thoracoplasty with No Operative Mortality

RICHARD H. DIEFFENBACH AND ANTHONY D. CRECCA

These 100 consecutive cases of thoracoplasty with no operative mortality were operated upon during the period 1936–1938 and the patients to date have been followed from three to five years. There were 221 operations on these 100 patients.

The following is a summary of the number of stages and the results in relation to negative sputum.

100 cases: A total of 221 operations

15 cases: One stage only	12 negative sputum
65 cases: Two stages	43 negative sputum
18 cases: Three stages	14 negative sputum
22 cases: With revision operation	14 negative sputum

Summary of the results in relation to concurrent and previous collapse therapy follows:

Thoracoplasty results

With contralateral pneumothorax
41 cases: 23 negative; 5 died; 13 still positive sputum
With previous pneumothorax sputum
57 cases: 40 negative; 8 died; 9 still positive sputum
With no previous pneumothorax
31 cases: 27 negative; 1 died; 8 still positive sputum
With 2nd operation or revision
22 cases: 14 negative; 1 died; 7 still positive sputum

In 8 cases the presence of tuberculous empyema was the reason for thoracoplasty. The thoracoplasty was followed by a Schede operation. In this group 7 patients had *empyema necessitatis*. All 8 had bronchopleural fistula. Three patients represented standovers from the old Sauerbruch thoracoplasty and a complete secondary operation had to be performed in each case.

The following summarizes the results as related to the existing disease at the time of operation.

Pathology

With contralateral caseous pneumonic lesion
38 cases: 21 negative; 7 died; 10 still positive sputum
With contralateral exudative productive lesion
14 cases: 10 negative; 2 died; 2 still positive sputum
With contralateral proliferative lesion
30 cases: 23 negative; 1 died; 6 still positive sputum
With previous pleural effusion
31 cases: 22 negative; 4 died; 4 still positive sputum

No vascular accidents occurred in this group.

Horner's syndrome occurred in 4 cases. This condition, we feel, is due to trauma of the sympathetic chain during mobilization of the lung. It has persisted with slight improvement in all cases.

There was one brachial plexus injury with parasthesia along the ulnar nerve; this subsequently disappeared.

Pleural tears happened in 4 cases. The complications following this were combated by postoperative deflation of the resulting pneumothorax and attempt to suture the tear with intercostal muscle and fascia.

In this group there are 50 males and 50 females (91 whites, 8 Negroes and one of the yellow race). The age groups are given in the following tabulation. Seventy-one cases are arrested with negative sputum and closed cavities; the patients are working or able to work. Sixteen patients still have positive sputum. Thirteen died from progression of disease.

Age Group	*Number of Patients*
14–20	9
21–30	47
31–40	30
41–50	14

Analysis of 104 Cases of Thoracoplasty

GEORGE G. FINNEY

Analysis of 104 cases of thoracoplasty for pulmonary tuberculosis, covering a period from April, 1932 to December, 1940, is presented. This is a consecutive series operated upon by Dr. Robert T. Miller and the author. The present status of the patients is given as reported by the physicians of the various sanatoria where convalescence took place following surgery. Follow-up has been obtained in nearly 100 per cent of the cases.

Particular consideration is given not only to the operative and ultimate mortality, the types of cases and number of operations, but also to the incidence of infection, since no special precautions were taken at operation other than scrupulously careful surgical technique. Type of operation done is described and also the importance of the position used on the operating table is stressed, with special reference to a small axillary pillow used to aid free respiratory movements.

The necessity for good anaesthesia is brought out, cyclopropane gas having been found very satisfactory.

The benefit of routine blood transfusion, started during the operation and continued until the patient is conscious in order to avoid the usual postoperative drop in blood pressure, is stressed.

Results of Thoracoplasty

H. MELTZER

A series of 181 cases of thoracoplasty operated on over the five-year period 1935–1940 is presented. The total is made up of one minimal, 31 moderately advanced and 149 far advanced cases, including 25 with empyemata complicating their pulmonary disease. One hundred and thirty-six of the far advanced cases had bilateral disease, and 30 of these had contralateral collapse. The contralateral collapse consisted of 20 pneumothoraces, 7 apicolyses combined with paraffin packs, 2 phrenic nerve evulsions and one bilateral thoracoplasty.

The 181 cases are further classified as: acute, 12 cases; subacute, 30 cases; chronic, 139 cases. The chronic cases are again divided into "good chronics," 72 cases; "bad chronics," 42 cases and chronics with empyema, 25 cases; this latter subgroup is made up of 17 pure tuberculous empyemata and 8 with mixed infection. Results in each group and subgroup are analyzed.

Ninety-two cases had thoracoplasty done on the right side, 89 on the left; 92 were males, 89 were females; the average age of males was 32.3 years, of females 29.9 years.

The multiple-stage posterior operation of Alexander was employed in all cases; 98 had anterior collapse supplementing the posterior stages; 12 had supplementary extrafascial apicolysis; 18 had scapulectomy in lieu of additional rib removal; the 8 mixed infection empyema cases required additional Schede-type revision.

Local anaesthesia was used exclusively in the 560 stages required for the 181 cases. One-half of one per cent novocaine solution with 2 minims of epinephrine 1:1000 added to each ounce was found most satisfactory. In one instance only were flushing, dizziness, rapid pulse and dyspnoea due to the anaesthetic noted and then not in prohibitive degree. In earlier operations 750 cc. of solution were used; in more recent operations 300 to 450 cc. were found adequate. Local anaesthesia has advantages over general anaesthesia: (*1*) the necessity of gentleness in handling tissues, (*2*) greatly reduced bleeding due to the action of epinephrine, (*3*) the opportunity for greater care in controlling bleeding, and (*4*) uninterrupted presence of the cough reflex; *1*, *2* and *3* minimize shock; *4* minimizes the danger of sputum blockage which might lead to atelectasis and or spread of disease. Local anaesthesia is considered to have been an important factor in attaining the favorable results presented.

Seven-rib thoracoplasties averaged 140 cm. in length of ribs removed; this indicates the completeness of rib-removal employed and completeness of removal is also considered to have been an important factor in attaining favorable results.

Accidents attributable to operation included: 7 minor degrees of shock; 8 minor pleural tears that healed without misadventure; 6 cases of paradoxical respiration with one death; 8 instances of wound infection with one proving fatal; one case of respiratory failure with fatal outcome; 3 cases of moderate atelectasis with good recovery in each. Thus there was an early operative death rate of

3, or 1.6 per cent. Six cases had extension of disease following operation and of these 5, or 2.7 per cent, ultimately died; 7 other deaths from nontuberculous causes occurred remotely after operation, giving a total of 15, or 8.2 per cent, dead from all causes at the end of the five-year period.

One hundred and forty-three cases (79 per cent) had been nonbacillary for at least six months postoperatively on examination by sputum specimen, gastric contents and culture; 115 cases had been discharged to their homes and of these, at the end of the five-year period, 5 were dead from nontuberculous causes; 14 had had reactivation and were readmitted; 3 were classified as still active but not readmitted; 13 were quiescent; 20 were apparently arrested; 56 were arrested and 4 were apparently cured. Fifty-eight were working or able to work at least part time.

Analysis with regard to various factors gives the following results:

(*1*) Contralateral collapse with thoracoplasty is well tolerated and gives favorable results.

(*2*) Best results are obtained in the twenty-one to thirty year old group but middle-age is not a contraindication in well selected cases.

(*3*) Most favorable results are obtained in cases where disease has been present for four months to four years; cases with disease of ten years' standing show a marked decline in good results; cases with acute disease of less than four months' standing show the poorest results of all but, considering that these were classed as hopeless without operation, the results obtained merit further trial of thoracoplasty in the acute rapidly progressive type of case.

(*4*) Amount of disease plays a very important part in results; although the far advanced bilateral group shows 73.5 per cent nonbacillary, yet all the recorded deaths occurred in this group.

(*5*) Type and duration of preceding pneumothorax has little influence on results. Length of hospitalization and ultimate results seem better in those without previous pneumothorax.

(*6*) Extent of cavitation bears a direct relation to results; the greater the cavitation the worse the results.

(*7*) There are 166, or 91.8 per cent, living patients in the entire group and, of these, 143, or 86.1 per cent, are bacilli free.

Thoracoplasty in Bilateral Pulmonary Tuberculosis

ARTHUR M. VINEBERG, DOUGLAS ACKMAN AND MICHAEL ARONOVITCH

Fifty cases of bilateral pulmonary tuberculosis which had had unilateral thoracoplasty were reviewed and analyzed in an effort to discover why certain of them did well while others did not. Cases with well healed disease on the contralateral side were not included.

The contralateral side at the time of operation was classified in each case as retrogressing, quiescent or progressing, with or without cavity. This classification was based mostly on serial X-ray evidence over variable periods of time prior to operation.

Most favorable results were obtained in those cases which showed actively retrogressing disease even if the retrogression had been going on for only a short period of time. The so-called quiescent cases did not do quite as well. Those cases with progressive disease on the contralateral side gave poor results.

Results in Ninety Consecutive Thoracoplasties

ARTHUR H. AUFSES

The results of thoracoplasties for pulmonary tuberculosis upon 90 consecutive patients, from January 1, 1935 to July 1, 1940, are analyzed. All patients had positive sputum and visible cavitation prior to operation. Some were complicated by undrained tuberculous empyema. Eighty per cent of the patients were between the ages of twenty and forty years and a high percentage had long-standing disease.

The contralateral lung was considered inactive at the time of operation, but approximately 30 per cent had X-ray evidence of bilateral tuberculosis. Other measures rather than thoracoplasty are used in patients presenting active lesions in both lungs.

The classical upper selective thoracoplasty with complete resection of the first three ribs was used in practically all cases. One hundred and ninety-two operations were performed. Thirteen patients had one-stage procedures; 57 had two stages; 15 had three stages and 5 had four stages. In 37 patients a Semb extrafascial apicolysis was performed in addition to the rib resection.

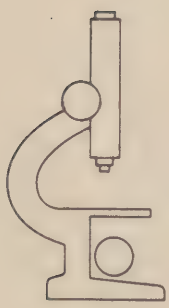
The follow-up is from one to six years' duration and every case has been followed to date. There are 71 per cent arrested; 18 per cent not arrested; 7 per cent postoperative deaths and 4 per cent late deaths. The classification "arrested" conforms to the standards set by the National Tuberculosis Association.

Of special interest is the rehabilitation of the arrested cases. Of 43 patients operated upon before January 1, 1939, and discharged as arrested, 41 are working full time or doing their housework. This high percentage of rehabilitated patients is credited in part to the duration of postoperative sanatorium care and later graded hourly increases in work under medical supervision.

The 6 postoperative deaths were due to pneumonia, transfusion reaction, phlegmonous infection of the wound, pheochromocytoma of the adrenal and contralateral pulmonary atelectasis.

The reasons for failure were attributed to a long standing hard fibrotic pulmonary lesion in 6 patients and an abnormally long delay between the first and second stages in 5 patients.

The relation of the status on discharge to the present status shows that of those patients discharged as arrested only 4 turned positive later. On the other hand, 6 of those discharged with positive sputum are now arrested. This is in marked contrast to the results obtained by supplementary operations, such as, anterior costectomies and posterior revisions, the results of which were far from gratifying.



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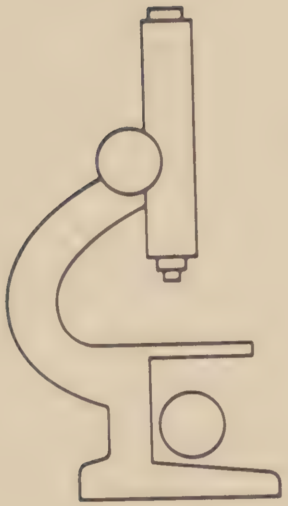

SURGERY

PULMONARY RESECTION IN THE TREATMENT OF PULMONARY TUBERCULOSIS[1,2]

RICHARD H. OVERHOLT AND NORMAN J. WILSON

During the past decade pulmonary resection as a form of treatment for pulmonary tuberculosis has been applied to a steadily increasing number of patients. In the earlier years of this period results were discouraging because of the relatively high operative mortality and the prohibitive incidence of serious complications, such as contralateral spread, empyema and bronchial fistula. However, progress has been rapid in the field of thoracic surgery in the past few years so that the entire picture has changed and become more hopeful. Newer and better operative techniques have been developed, especially the individual ligation of the hilar structures and the pleural flap method of reinforcing the bronchial closure. Rapid strides have also been made in the allied fields of anesthesiology and bronchoscopy. Intratracheal anesthesia administered by trained anesthetists has enabled the thoracic surgeon to perform tasks that otherwise would have been impossible. Bronchoscopy has revealed the high incidence of bronchial tuberculosis. This has permitted a more intelligent approach to pulmonary resection in these cases and has prevented many of the mistakes and failures experienced in the earlier years. A new era of chemotherapy of infection was also ushered in with the advent of the sulfonamides and, more recently, penicillin. All of these improvements have steadily reduced the mortality and complications associated with lung resection. In fact, pulmonary resection can be performed to-day with such a margin of safety that it should be considered in any therapeutic program in treating tuberculous patients.

Since 1934, 97 pulmonary resections have been performed in the treatment of tuberculosis by one of us (R. H. O.). The present report deals with the 60 operations performed between January 1, 1942, and January 1, 1944.[3] The 18 patients operated on prior to this time have been omitted because during the early years the operative technique and the criteria for the selection of patients were not well standardized. During that time the pleural flap method of closing the bronchus was not routinely used and in a few cases the tourniquet method of handling the hilum was employed. The patients operated on since January 1, 1944 have been omitted because the follow-up period has been too short to permit evaluation of their condition.

GENERAL STATISTICS

Table 1 presents the general statistics. Sixty resections were performed upon 59 patients. One patient had two lobectomies. There were 36 pneumonecto-

[1] From the New England Deaconess Hospital, Boston, Massachusetts.

[2] Presented before the Medical Section at the 40th annual meeting of the National Tuberculosis Association, Chicago, Illinois, May 11, 1944.

[3] An inclusive report on all patients treated by resection between 1934 and July 1, 1943 has been submitted for publication (5).

mies, 14 on the right and 22 on the left; and 24 lobectomies. We should like to call special attention to the 6 left upper lobectomies. These were all performed with individual ligation technique without any unusual technical difficulties.

TABLE 1

General statistics

I	Number of patients			59
II	Number of resections			60
	A. Pneumonectomies		36	
	1. Right	14		
	2. Left	22		
	B. Lobectomies		24	
	1. Right upper	6		
	2. Right upper and middle	2		
	3. Right lower and middle	1		
	4. Right lower	5		
	5. Left upper	6		
	6. Left lower	4		
III	Preoperative classification			
	A. Reasonable risks		47	
	B. Desperate risks		13	
IV	Age of patients—15 to 54 years			
	A. 15 to 20		1	
	B. 20 to 30		23	
	C. 30 to 40		26	
	D. 40 to 50		5	
	E. 50 to 55		4	
V	Sex			
	A. Females		38	
	B. Males		21	
VI	Duration of illness			
	A. Under 6 months		6	
	B. 6 months to 1 year		8	
	C. 1 year to 2 years		16	
	D. 2 years to 3 years		7	
	E. 3 years to 4 years		7	
	F. 4 years to 5 years		5	
	G. 5 years to 10 years		6	
	H. 10 years to 15 years		4	
	I. 19 years		1	
VII	Incidence of tuberculous bronchitis—31.7 per cent (19 cases)			
	A. Submucosal type		1	
	B. Ulceration		5	
	C. Ulcero-stenosis		9	
	D. Fibrous stenosis		4	
VIII	Incidence of positive sputum—90 per cent (54 cases)			

Our experience here is contrary to that of Kent and Blades (3) who stated in 1942, with reference to the left upper lobe, "Except under unusually favorable circumstances, individual ligation technique for resection will be hazardous or impossible."

The patients were classified preoperatively according to the risk involved. Thirteen were classified as desperate risks. These were patients in whom an early fatal course was anticipated. Not only in our opinion, but in the opinion of every physician concerned, pulmonary resection offered them their only chance to get well. The reader is referred to table 8 for details concerning these cases. Analysis of this table will reveal that 11 had active progressive tuberculosis, 8 had tuberculous bronchitis and 2 had contralateral lesions involving the upper third of the lung. One patient, who had previously had extensive thoracoplasty, had a vital capacity of 900 cc. before left pneumonectomy was performed. One had had pulmonary tuberculosis for nineteen years.

There were 47 patients classified preoperatively as reasonable risks. We do not wish to infer by this classification that these patients had stabilized forms of tuberculosis or that the operation was elected in preference to thoracoplasty. On the contrary, the vast majority of these patients had extensive, active, progressive tuberculous lesions. In 32 patients thoracoplasty was either considered to be contraindicated or failure was anticipated. In our opinion, thoracoplasty might have been used with some hope of success in only 15 of the cases.

The remainder of the table is self-explanatory. We should like to call attention, however, to the very high incidence of tuberculous bronchitis, which was present in 31.7 per cent; also to the high incidence of positive sputum, 90 per cent. The 6 patients who had negative sputum at the time of resection are represented by the following:

1: One patient previously had tuberculosis in the right lower lobe which was controlled by pneumothorax. The resection was performed for residual bronchiectasis involving the right lower and middle lobes.
2: One whose tuberculosis had been controlled by an extensive left thoracoplasty still was incapacitated by recurring pulmonary hemorrhages. Her vital capacity was 900 cc. at the time of operation.
3: One had pulmonary tuberculosis for ten years and a right pneumothorax for four years. A slowly progressive lesion was present in the left upper lobe which at the time of resection involved almost the entire lobe. In spite of this extensive disease, a positive sputum was never secured from the patient (except once in January, 1943). (See figure 2.)
4: One patient had an extensive involvement of the right lower lobe which had been partially controlled by pneumothorax. However, after three years of pneumothorax, the sputum was still intermittently positive and frequent hemoptyses occurred. For this reason, the small, opaque, right lower lobe was resected.
5: One had pneumothorax for several months. The sputum had been converted, but his lung had become opaque and unexpandable. Fluid formed in the pleural space which was positive for tubercle bacilli on guinea pig inoculation.
6: One patient had a tuberculoma in the right upper lobe.

Table 2 presents the indications for the 60 resections. Associated suppurative disease was the indication in 2 cases. Both had bronchiectasis. The tuberculosis was apparently arrested in one and was active in the other.

Uncontrolled disease following thoracoplasty was the indication in 9 cases. One-third of this group had endobronchial tuberculosis. Two of these patients previously had a revisional thoracoplasty. Resection was performed in preference to a revisional thoracoplasty in 5. In the remaining 2 cases, revisional

TABLE 2

Indications

I	Associated suppurative disease—2 cases	
	A. Tuberculosis controlled	1
	B. Tuberculosis uncontrolled	1
	Total	2
II	Post-thoracoplasty uncontrolled disease—9 cases	
	A. No endobronchial tuberculosis	6
	B. With endobronchial tuberculosis	3
	Total	9
III	Extensive multilobar predominantly unilateral tuberculosis—29 cases	
	A. No endobronchial tuberculosis	13
	B. With endobronchial tuberculosis	16
	Total	29
IV	Extensive upper lobe tuberculosis—8 cases	
	A. No endobronchial tuberculosis in this group	
V	Basal tuberculosis—9 cases	
	A. No endobronchial tuberculosis in this group	
VI	Recurrent hemorrhages—tuberculosis controlled with thoracoplasty—1 case	
VII	Tuberculoma—1 case	
VIII	Giant cavities in both upper lobes—1 case	

thoracoplasty was considered to be contraindicated because of a flaccid chest wall in one and because of an extensive spread to the lower lobe following the initial thoracoplasty in the other. Four of the patients in this group were treated by lobectomy and 5 by pneumonectomy.

The most common indication in this group was extensive multilobar disease which was predominantly unilateral. This was present in 29 patients, all of whom were treated by pneumonectomy. Sixteen had tuberculous bronchitis involving the major bronchi. Extensive thoracoplasty as an alternative form of treatment might have been used with doubtful results in only 7 patients of this

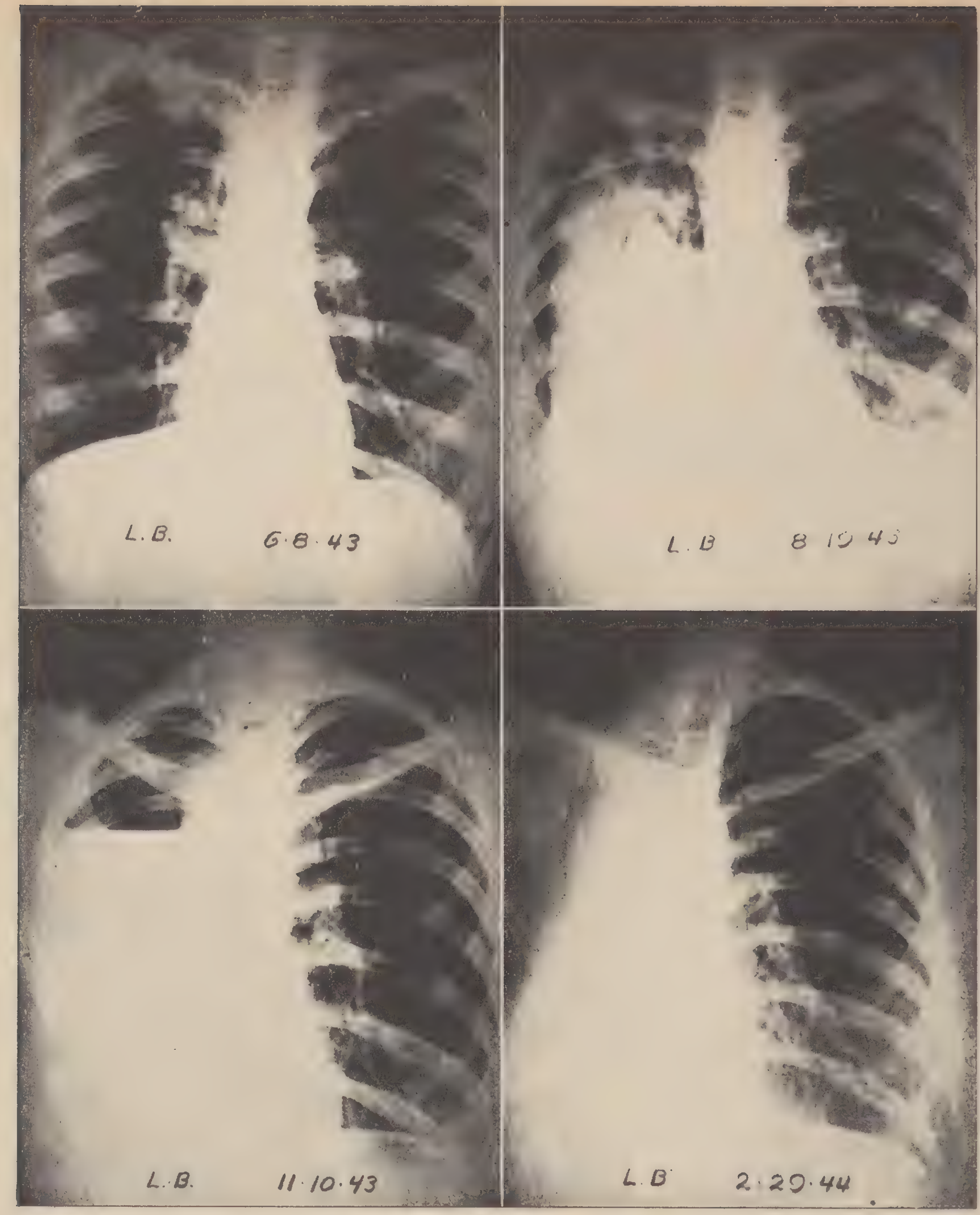

FIGURE 1A

Mrs. L. B. Age twenty-three. Case #70 in table 8. Onset of tuberculosis eight months prior to resection. Right pneumothorax instituted in July, 1943. Right lung became opaque. Bronchoscopy negative. Right pneumonectomy performed on October 11, 1943. Patient had an uneventful postoperative course. Has been asymptomatic since operation and her sputum has been consistently negative, including guinea pig inoculation.

Upper left: Roentgenogram of June 8, 1943 showing exudative lesion with small cavity at right apex and a small amount of infiltration near the hilum. Left lung clear.

Upper right: Roentgenogram of August 19, 1943, shortly after the induction of right pneumothorax. Note the dense opacity involving the major portion of the right lung and the cavity at right apex. A small nodular spread is present in left lung in middle third.

Lower left: Roentgenogram one month following right pneumonectomy.

Lower right: Roentgenogram of February 29, 1944, four and one-half months following resection.

entire group. In the remaining 22, the failure of thoracoplasty was anticipated or thoracoplasty was actually considered to be contraindicated.

Extensive tuberculosis of the upper lobe was the indication in 8 cases. There was no involvement of the major bronchi in this group. All cases were treated by lobectomy except one. In this patient a pneumonectomy was performed because of extensive involvement of the superior division of the left lower lobe.

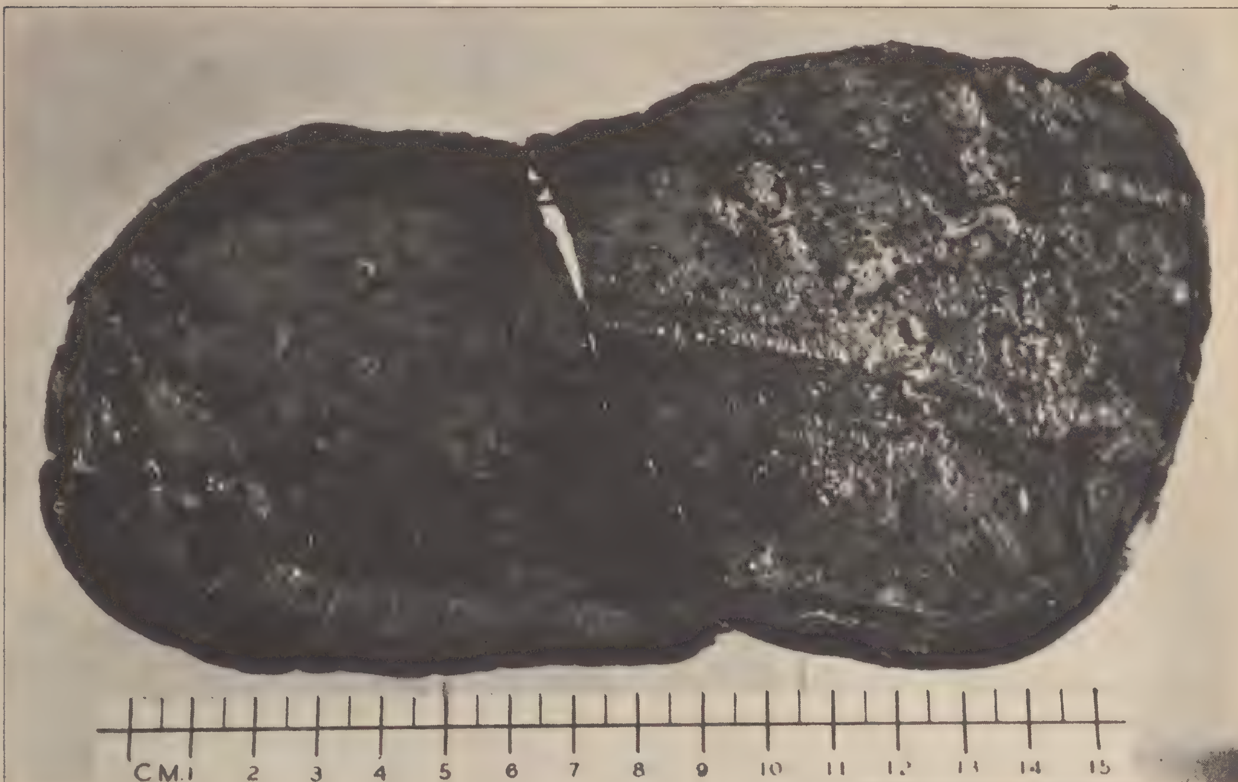

FIGURE 1B

Surgical specimen (right lung) which revealed extensive involvment of the entire lung with nodular caseous foci measuring up to 0.6 cm. These were predominantly in the upper and lower lobes. There was moderate involvement of the middle lobe. There was extensive involvement of the bronchi throughout the lung. The bronchial segment adjacent to the bronchial suture line revealed submucosal tubercles. The pleura was only slightly thickened.

Note: This specimen shows that the dense opacity which developed suddenly following pneumothorax was not atelectasis but, in reality, an involvement of almost the entire lung by tuberculous nodules.

This was first discovered at surgical exploration as it had not been revealed by X-ray study.

Basal tuberculosis was the indication for resection in 9 cases. Eight were treated by lobectomy and one by pneumonectomy. Resection was used as a primary form of therapy in 3 of these patients. Another had had a short-term pneumothorax which was ineffective, and resection was performed without fur-

ther delay. Two had failed to control their disease with phrenic paralysis. One had residual symptoms and intermittent positive sputum after three years of pneumothorax. The remaining patient had residual symptoms and positive sputum after five years of pneumothorax and several phrenic crushes.

Recurrent hemorrhages were the indication in one and tuberculoma in one. The indication in the remaining case was bilateral giant cavities in the upper lobes. A bilateral upper lobectomy has been performed on this patient, the last resection having been done in January, 1944.

It is very difficult to present the indications for resection completely for each case. Many of the patients had failed to respond to pneumothorax, phrenic paralysis, or both. In others, pneumothorax was impossible because of pleural symphysis. For more detailed information concerning these cases, the reader is referred to table 8.

COMPLICATIONS

In 1942, Thornton and Adams (6) collected from the literature records of 29 pneumonectomies and 46 lobectomies. In this collected series there was a very high incidence of serious complications, particularly persistent fistula, contralateral spread and empyema. Table 3 presents a comparison between this collected series of Thornton and Adams and the 60 resections presented in this paper. This table is presented to show the progress made in the last few years, and is in no way meant to be a criticism of the earlier workers and pioneers in this field. An analysis of this table shows that two of the complications, namely, persistent fistula and empyema, have been eliminated in the 24 consecutive lobectomies. Persistent fistula occurred in only one of the 36 pneumonectomies. This fistula developed nine months following resection in a patient who had been completely well and asymptomatic up until this time. She also had, as one would suspect, a tuberculous empyema. Nontuberculous empyema occurred in 2 cases, or 5.5 per cent of the pneumonectomy cases. Both of these were caused by *Staphylococcus aureus*, and there was no evidence of tuberculous infection in either of them. The reduction in the incidence of persistent fistula and empyema has been accomplished by two important technical improvements: (*1*) the individual ligation technique of handling the hilar structures, and (*2*) the pleural flap method of closing the bronchus. The high incidence of these complications in the earlier years was due not to the tuberculous infection *per se*, but to improper technique.

Contralateral spread remains the most frequent complication and the greatest threat to the patient in resection for pulmonary tuberculosis. It occurred in 11.1 per cent of the 36 pneumonectomies and in 12.5 per cent of the 24 lobectomies. As can be seen, the incidence of this complication varied little with the type of operation. In our opinion, it is more a manifestation of the type of disease the patient has, and is more apt to occur when a large amount of secretion is present. It is caused by contralateral spilling of secretions during the operative procedure. In recent months an attempt has been made to overcome this complication. An attempt is made to ligate the bronchus as a primary step in the operation whenever it is technically possible. It is also important that the anesthetist keep

the patient in an even plane of anesthesia to prevent deep gasping breaths, and to pay strict attention to the aspiration of all secretions throughout the operation.

TABLE 3

Complications

	THORNTON AND ADAMS COLLECTED SERIES	60 RESECTIONS (OVERHOLT) JAN. 1942 TO JAN. 1944
Pneumonectomy	*29 Cases*	*36 Cases*
1. Persistent fistula	34%	2.7%
2. Contralateral spread	24%	11.1%
3. Empyema without fistula	17%	5.5% (2 cases —both nontuberculous)
Lobectomy	*46 Cases*	*24 Cases*
1. Persistent fistula	39%	0%
2. Contralateral spread	25%	12.5%
3. Empyema without fistula	25%	0%

TABLE 4

Complications

I Complications related to the tuberculous infection

COMPLICATIONS	PNEUMONECTOMY (36)		LOBECTOMY (24)		TOTAL (60 CASES)	
	Cases	Per cent	Cases	Per cent	Cases	Per cent
Wound infection	0	0	0	0	0	0
Tuberculous empyema	1	2.7	0	0	1	1.6
Nontuberculous empyema	2	5.5	0	0	2	3.3
Temporary fistula	0	0	1	4.1	1	1.6
Permanent fistula	1	2.7	0	0	1	1.6
Contralateral spread	4	11.1	3	12.5	7	11.6
Ulceration of bronchial stump	4	11.1	1	4.1	5	8.5
Contralateral exacerbation	3	8.3	0	0	3	5.0
Contralateral lesion developing late	1	2.7	0	0	1	1.6
Contralateral pleurisy with effusion	1	2.7	0	0	1	1.6
Tuberculosis of chest wall	3	8.3	0	0	3	5.0
Ipsolateral spread	—	—	2	8.2	—	—
Ipsolateral exacerbation	—	—	2	8.2	—	—

II Complications related to surgical problem of pulmonary resection:

A. Paroxysmal irregular heart action with sudden death	1
B. Circulatory collapse	1
C. Embolism	1
D. Postoperative shock	1
E. Pulmonary insufficiency	1

Table 4 presents a summary of all complications. There were no wound infections. A temporary fistula occurred in one patient following lobectomy. This was closed with a muscle transplant. A limited thoracoplasty was then performed. The patient did not develop an empyema. To-day he is clinically well and has a consistently negative sputum. (See figure 2.)

FIGURE 2A

Figure 2A

Mr. W. K. Age twenty-two. Case #51 in table 8. Patient had been under treatment for tuberculosis for ten years. Right pneumothorax had been present for four years and had controlled the lesion in the right lung. The lesion in the left upper lobe had slowly progressed for two years. A positive sputum was found in January, 1943. At no other time was a positive sputum secured. Left upper lobectomy was performed on March 22, 1943. The patient developed a small fistula postoperatively. On May 11, 1943, a left thoracoplasty was performed. At the same time the pleural space was opened and a muscle transplant was sutured over the fistula. An empyema did not develop. The pleural space became obliterated. The patient is asymptomatic and well. His sputum is consistently negative on concentration. Gastric specimen is also negative.

Upper: Roentgenogram of March 4, 1943, showing right pneumothorax and infiltration in left upper lobe.

Centre: Roentgenogram of May 3, 1943, six weeks following resection. Note the air and small fluid level in left pleural space.

Lower: Roentgenogram of March 20, 1944. The right lung has been reëxpanded. The left lung has also reëxpanded. Left lower lobe appears normal.

Ulceration of the bronchial stump occurred in 4 patients following pneumonectomy, and in one following lobectomy, a total incidence of 8.5 per cent. This complication occurs much more frequently than one would suspect from the reports in the literature. It can be diagnosed only by routine bronchoscopic examination following operation. It may occur early or late in the postoperative period. We have discovered one case ten months following resection. For

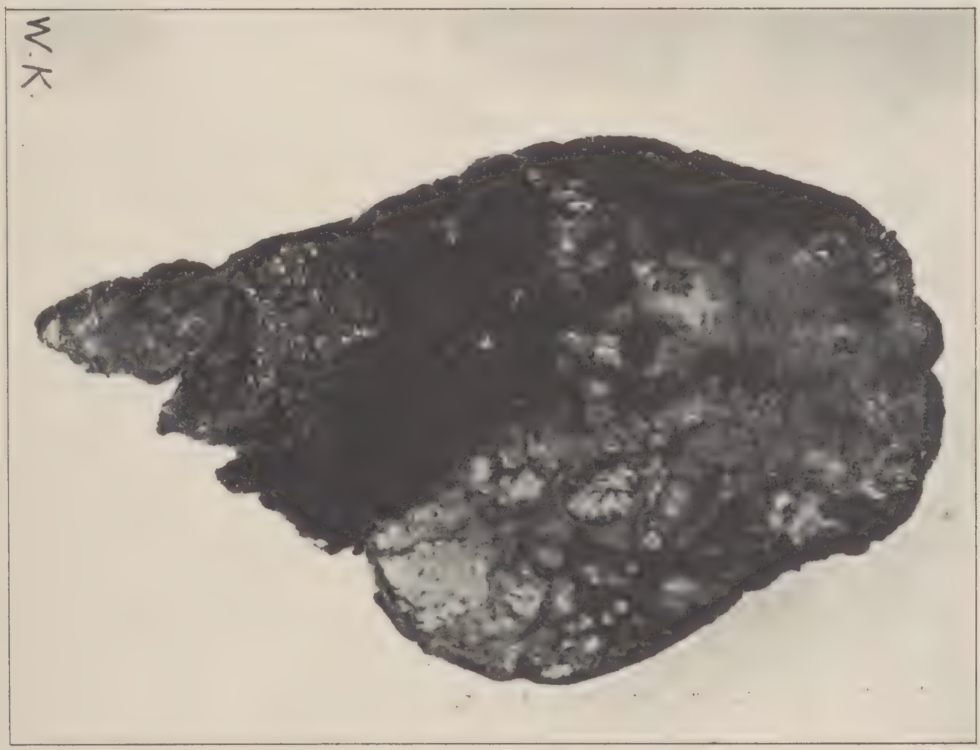

Figure 2B

Surgical specimen (left upper lobe) showing extensive involvement with caseous nodules of the entire lobe except for the lingular segment. No cavities found. The smaller bronchi were involved.

this reason we now advocate a routine bronchoscopic examination six weeks following resection and a repetition of this in six months if the first examination is negative. Persistence or recurrence of positive sputum may indicate stump involvement and calls for bronchoscopy. Stump ulceration must be considered as a possible source of infection in late spreads. Stump ulcers have been treated with 30 per cent silver nitrate every two weeks with gratifying results. Three of them have cleared so that at the present time there is no evidence of activity in the bronchial stump. Two of these patients are negative on guinea pig inoculation and the other is positive by guinea pig inoculation. A fourth case has been treated irregularly. She still has active ulceration in the bronchial stump and her sputum is positive. The ulcer which occurred in the lobectomy patient progressed; further resection was performed and pneumonectomy was completed. At the present time she is clinically well, although her sputum is positive on guinea pig inoculation.

Contralateral exacerbation occurred in 4 pneumonectomy patients and in none of the lobectomy cases. Two of these occurred in the postoperative period. One patient died as a result of this exacerbation and the other patient now has a stabilized lesion. At the present time he is clinically well, and is ready for discharge from the sanatorium. The third patient developed contralateral exacerbation eight months following pneumonectomy. A fourth developed a contralateral lesion eighteen months following operation. An evanescent lesion had been present in this location three months before, but this had entirely cleared before the pneumonectomy had been performed. This lesion progressed rapidly and caused the death of the patient. We believe that these contralateral exacerbations have been related not to the type of operation performed but entirely to the type and extent of preëxisting disease.

One patient developed a contralateral pleurisy with effusion three months following pneumonectomy. The pleural fluid was negative by guinea pig inoculation. This patient is at home, is well, and has a negative sputum on all tests except for guinea pig inoculation of the gastric specimen. A parenchymal lesion has never developed in the underlying lung.

In 3 patients concealed tuberculosis of the chest wall was found. These were very interesting and instructive cases. Following pneumonectomy the wound healed by primary intention in all 3, and at no time was there any indication of the underlying involvement. These patients returned for thoracoplasty and, after the incision had been made, granulation tissue was found in the soft tissues of the chest wall. Biopsy of this material revealed tissue changes consistent with tuberculosis. In spite of this, the operation was continued and thoracoplasty completed. The wound again healed by primary intention and remained healed in all 3 cases. They are all clinically well and have negative sputa at the present time.

Ipsolateral spread occurred in one patient in the postoperative period and in another case, eight months after resection. In the second instance the spread was a direct result of ulceration in the stump of the bronchus. Both cases had

extensive involvement of the bronchi on pathological examination. Ipsolateral exacerbation occurred in 2 lobectomy patients. In one, a cavity developed in the superior division of the lower lobe a few weeks following resection of the upper lobe. In the other, a fine nodular infiltration was found in the middle lobe. At the time of exploration the extent and character of the lesion hardly seemed to justify a sacrifice of this lobe. However, the lesion progressed a few months after resection.

Section 2 of table 4 deals with the complications related to the surgical problems of pulmonary resection rather than those associated with the tuberculous disease. These complications contributed to the death of the patient in each instance. This part of the table is self-explanatory.

TABLE 5

Fatality statistics

I Operative fatality—60 resections		
Total		11.6% (7 of 60)
A. Reasonable risks	4.3% (2 of 47)	
B. Desperate risks	38.5% (5 of 13)	
II Case fatality—59 patients		
Total		13.6% (8 of 59)
A. Reasonable risks	6.5% (3 of 46)	
B. Desperate risks	38.5% (5 of 13)	

Note: One late death in this group of cases.

FATALITY STATISTICS

Table 5 presents fatality statistics. The cases have been divided, as previously described, into reasonable and desperate risks. The total operative fatality was 11.6 per cent, there being 7 deaths following 60 operations. The operative fatality for the reasonable risk cases was 4.3 per cent, representing 2 of the 47; that for the desperate risk was 38.5 per cent, representing 5 of the 13. The case fatality statistics vary little with the operative fatality because of the fact that there was only one late death in this entire group.

Table 6 analyzes the postoperative deaths. Five of the 7 patients who died in the postoperative period had been classified preoperatively as desperate risks. Five had a complicating tuberculous bronchitis. The analysis of the cause of death in these cases is quite interesting. Only 2 of the patients died of complications related to the tuberculosis. One of the reasonable risk cases died of a contralateral tuberculous pneumonia, and one of the desperate risk cases died of contralateral exacerbation associated with pulmonary insufficiency. The remaining 5 patients died of complications related to the surgical problem of pulmonary resection. Four of these were in very poor general condition prior to the operation.

As stated before, there was only one late death in this group. This occurred

in a fifteen-year-old female who developed an acute, rapidly spreading tuberculous lesion in the contralateral lung eighteen months following resection.

The analysis of these fatality statistics permit the following conclusions:

1: The operative fatality in reasonable risk cases is 4.3 per cent.
2: The operative fatality in desperate risk cases is quite high, being 38.5 per cent in this series.
3: Seventy-one per cent of the postoperative deaths have occurred in those classified preoperatively as desperate risks.

TABLE 6

Analysis of postoperative deaths

	NAME	AGE	OPERATION	PREOPERATIVE CLASSIFICATION		DURATION OF ILLNESS	TUBERCULOUS BRONCHITIS	POST-OPERATIVE DAY OF DEATH	CAUSE OF DEATH
				Desperate risk	Reasonable risk				
1	Miss T. B.	24	Lt. upper lobectomy		Yes	22 months	0	5	Contralateral tuberculous pneumonia
2	Miss S. A.	25	Lt. pnectomy	Yes		5 months	0	1	Paroxysmal irregular heart action with sudden death
3	Mrs. M. M.	32	Rt. pnectomy	Yes		2¼ years	Yes	2	Circulatory collapse
4	Mr. J. C.	54	Lt. pnectomy	Yes		4 years	Yes	53	Contralateral exacerbation, pulmonary insufficiency
5	Mrs. A. B.	39	Rt. pnectomy		Yes	11 years	Yes	15	Embolism
6	Miss M. F.	30	Rt. pnectomy	Yes		3 years	Yes	2 hours after op.	Postoperative shock
7	Mr. J. G.	49	Rt. pnectomy	Yes		19 years	Yes	19	Pulmonary insufficiency

4: Only 2, or 28.5 per cent of the postoperative deaths, have been due to the tuberculosis *per se.* The remainder of the postoperative deaths have occurred as a result of complications incident to the surgical procedure. These have occurred, with the exception of one case, in patients in very poor general condition.
5: The incidence of late deaths has been very low to date, there being but one death among the group of 52 patients who survived the two-month postoperative period.

COMPARATIVE RESULTS OF REASONABLE RISK CASES TREATED BY LOBECTOMY AND PNEUMONECTOMY

Table 7 analyzes the results in the reasonable risk cases. There were 25 patients treated by pneumonectomy and 22 by lobectomy. Part one of table 7

gives the most common complications encountered in these two groups. In the 22 cases treated by lobectomy, there were no permanent fistulae, no tuberculous empyemata and no nontuberculous empyemata. In the 25 patients treated by pneumonectomy, one developed a permanent fistula and tuberculous empyema. Two others had postoperative empyemata caused by *Staphylococcus aureus* which were controlled by thoracoplasty. Several factors may account for the absence

TABLE 7

Comparative results in reasonable risk cases—lobectomy and pneumonectomy

		PNEUMONECTOMY—25 CASES		LOBECTOMY—22 CASES		TOTAL—47 CASES	
		Cases	Per cent	Cases	Per cent	Cases	Per cent
(A)	Complications						
	Permanent fistula	1	4	0	0	1	2.1
	Tuberculous empyema	1	4	0	0	1	2.1
	Nontuberculous empyema	2	8	0	0	2	4.2
	Contralateral spread	3	12	2	9.1	5	10.6
	Bronchial stump ulceration	2	8	1	4.5	3	6.3
(B)	Fatality						
	Operative fatality	1	4	1	4.5	2	4.2
	Total case fatality	2	8	1	4.5	3	6.3
(C)	Present Clinical Status						
	Clinically well with negative sputum	18	72	13	59.1	31	65.9
	Clinically well with positive sputum	2	8	2	9.1	4	8.5
	Residual symptoms (positive sputum)	2	8	—	—	2	4.2
	Fistula and empyema	1	4	0	0	1	2.1
	Dead	2	8	1	4.5	3	6.3
	Tuberculous involvement of remaining ipsolateral lobes	—	—	6	27.3	—	—
		(23 LIVING PATIENTS)		(21 LIVING PATIENTS)		(44 LIVING PATIENTS)	
(D)	Prognosis						
	Good	18	78.2	13	61.9	31	70.5
	Guarded	3	13	7	33.3	10	22.7
	Poor	2	8.7	1	4.8	3	6.8

of these complications following lobectomy. In the first place, the rapid reëxpansion of the lung after operation completely obliterates the pleural space and helps prevent the development of empyema. It also serves as an additional support to the area of the bronchial closure. The calibre of the sutured bronchi is much smaller and they are so located that less strain is exerted upon them when the patient coughs than in the case of a main bronchus.

Contralateral spread has occurred in 12 per cent of the pneumonectomy patients and in 9.1 per cent of those treated by lobectomy. This does not seem to be a significant difference.

Ulceration of the bronchial stump has occurred in 2 reasonable risk patients treated by pneumonectomy and in one of those treated by lobectomy. It is surprising that this complication should be so low in the patients treated by pneumonectomy, since 12, or 43 per cent, of this group had endobronchial tuberculosis visible through the bronchoscope. Both patients who developed this complication had an active endobronchial lesion in the orifice of the right upper lobe. Naturally, the bronchial closure was in the immediate vicinity of this involvement. The one patient treated by lobectomy who developed this complication was treated by right lower lobectomy. A study of the pathological specimen revealed extensive caseous involvement of the entire superior division bronchus. Undoubtedly that was the cause of this complication which might have been averted had a right middle and lower lobectomy been performed.

Section 2 of table 7 presents the fatality statistics. The operative fatality in both groups is almost identical, being 4 per cent in those treated with pneumonectomy and 4.5 per cent in those treated by lobectomy. There has been only one late death in either group, and this occurred in a patient treated by pneumonectomy. The total case fatality to date for the 25 patients treated by pneumonectomy is 8 per cent and for the 22 treated by lobectomy is 4.5 per cent.

Section 3 of table 7 presents the clinical status of both groups of patients. An analysis of this portion of the table will show that statistics for those treated by pneumonectomy are more favorable than for those treated by lobectomy: 72 per cent of the patients treated by pneumonectomy are clinically well and have a negative sputum,[4] whereas only 59.1 per cent of the lobectomy group fall into this classification. The remainder of this portion of the table is self-explanatory, except for the 6 lobectomy patients classified as having tuberculous involvement of the remaining ipsolateral lobes. Two of these patients have had spreads of residual disease. Three have residual open foci which were left behind at the time of operation. A bronchial stump ulcer was the source of spread in another. In our opinion, all 6 of these patients are failures because of the resection of too little lung tissue.

Section 4 of table 7 presents the prognosis of the 44 living patients. The prognosis is apparently good in 78.2 per cent of those treated by pneumonectomy and in 61.9 per cent of those treated by lobectomy. Of the 7 lobectomy patients with a guarded prognosis, it may be possible to change the status of 5 by further resection so that their prognosis may eventually be good. All patients classified as having poor prognosis will die of tuberculosis.

The lobectomy failures have been due to three factors which must always be considered:

1: Residual active foci remaining in the other lobes.
2: Spread of residual small foci which were considered inactive at time of resection.
3: Ulceration of the bronchial stump.

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[4] Results of cultures and guinea pig inoculations not included.

Our experience to date would indicate that it is dangerous to leave any significant amount of palpable or visible disease in the remaining lobes. These residual foci undergo some trauma during the operation and there is always some strain placed upon them during the reëxpansion of the lung.

The presence of tuberculous bronchitis is a definite hazard. Gross evidence of infection of a lobar bronchus should contraindicate lobectomy.

The statistics contained in this table are the most significant of any presented in this paper. They represent what pulmonary resection performed with modern technique offers the tuberculous patient who is in good general condition.

SPUTUM CONVERSION

The follow-up of this group of patients has been very difficult because the patients originated from so many different institutions and private physicians. In addition, the marked shortage of laboratory personnel has made a rigid study of the sputum impossible in a few instances. Of the 51 living patients, 14 are known to be positive on smear or concentration. With reference to the remaining 37 patients the following tabulation presents the results we now have concerning their sputum:

1: Twelve patients are negative on guinea pig inoculation of the sputum or gastric specimen.
2: In 3 patients the sputum is negative by culture.
3: The bronchoscopically aspirated specimen is negative in 5.
4: The gastric specimen is negative in 4.
5: Five patients are negative on concentration. Two of these are positive on guinea pig inoculation of the gastric specimen.
6: Six patients have been consistently negative on direct smear. All these patients are asymptomatic and clinically well. One of this group is positive by guinea pig inoculation of the gastric specimen.
7: Two patients have had no sputum examination since the time of resection. The reason for this is listed as "No cough or expectoration."

DESPERATE RISKS

Some may question the justification of separating statistics into desperate and reasonable risk groups. In fact, the advisability of accepting such desperate risk patients for resection may be questioned. However, we should like to distinguish between these patients and the poor risks described in various reports in thoracoplasty series. Those whom we have classified as desperate risks were otherwise utterly hopeless cases. In the opinion of every clinician taking care of them, resection offered them their only chance to get well. Thoracoplasty had already failed in 4, and in the remainder was considered to offer no chance of success in view of one or a combination of the following factors: bronchial involvement, giant cavitation, rapidly spreading and extensive parenchymal disease, prolonged and sustained toxemia and pyrexia, progressive weight oss or general debility. These patients meet the description of the desperate risk cases pictured by Alexander in his book *The Collapse Therapy of Pulmonary Tuberculosis*, for whom he advises against thoracoplasty. Any salvage in this group can be considered pure gain.

TABLE 8

Résumé of 60 consecutive pulmonary resections

	NAME	AGE	SEX	CASE NUMBER	PREOPERATIVE CLASSIFICATION	DATE OF OPERATION	INDICATION	ENDOBRONCHIAL TUBERCULOSIS	SPUTUM	DURATION OF DISEASE	PREVIOUS THERAPY: Contralateral lung	PREVIOUS THERAPY: Ipsolateral lung	OPERATION PERFORMED	COMPLICATIONS: Postoperative	COMPLICATIONS: Late	POSTOPERATIVE HOSPITAL DAYS	SPUTUM AT PRESENT	PRESENT CLINICAL STATUS
19	M. R.	40	F	1785	R. R.	1/ 6/42	I A	?	0	10 years	0	Pnthx., empyema Schede	Rt. M. & L.	0	0	30	Neg.	Well
20	E. M.	36	F	1907	R. R.	1/28/42	I B	?	+	7 months	0	0	L. L. L.	0	0	—	Neg.	Well
21	A. R.	32	F	1675	R. R.	2/19/42	III B	+	+	6 years	0	Pnthx.	Left pnectomy	0	0	27	Neg.	Well
22	E. A.	34	F	1172	R. R.	4/ 9/42	III B	+	+	2 years	0	Phrenic	Rt. pnectomy	0	Stump ulceration	20	Neg.	Well
23	R. B.	52	F	226	D. R.	4/27/42	VI	0	0	4½ years	0	Thpl., phrenic	Left pnectomy	0	0	23	Neg.	Well
24	M. S.	26	F	1634	R. R.	5/14/42	V	0	+	2 months	0	Phrenic	L. L. L.	0	0	18	Neg.	Well
25	D. B.	26	F	1900	R. R.	5/15/42	V	0	+	3 months	0	Pnthx.	R. L. L.	0	Stump ulceration, spread to rt. upper	14	+	Had R. U. & M. lobectomy in Jan. 1944
26	J. G.	28	F	1187	R. R.	6/18/42	V	0	+	2½ years	0	0	R. L. L.	Spread to rt. M. & U. lobes	0	21	+	Had rt. U. & M. lobectomy on 4/13/43
27	M. B.	28	F	1755	R. R.	6/29/42	IV	0	+	2½ years	0	Phrenic, pnthx.	L. U. L.	0	0	20	Neg.	Well
28	S. B.	15	F	1966	R. R.	7/17/42	III A	0	+	10 months	0	Pnthx.	Rt. pnectomy	0	Contralateral lesion 18 mos. later	18	—	Died Dec. 1943 of contralateral disease
29	P. H.	29	F	2094	R. R.	8/12/42	III B	+	+	8 months	0	0	Left pnectomy	0	Contralateral pleurisy with effusion	25	Neg.	Well
30	M. G.	29	F	1894	R. R.	8/25/42	V	0	+	17 months	0	Phrenic	R. L. L.	0	0	18	+	Clinically well. Sputum +
31	J. Y.	39	F	2154	R. R.	9/18/42	III B	+	+	3 years	0	Pnthx.	Left pnectomy	0	Contralateral lesion appeared May 1943	28	Neg.	Well
32	E. B.	35	F	2200	R. R.	10/ 9/42	I C	0	+	3 months	0	0	R. L. L.	0	0	27	+	Has residual disease in rt. U. & M. lobes. Has had thoracoplasty

33	M. S.	41	F	2194	R. R.	10/12/42	VII	0	0	2 years	0	0	R. U. L.	0	0	—	Neg.	Well
34	E. C.	25	F	2226	R. R.	10/23/42	V	0	+	3 months	0	0	L. L. L.	Contralateral spread	0	25	Neg.	Well
35	A. S.	30	F	889	D. R.	10/27/42	III A	0	+	6½ years	0	Pnthx., pnlysis	Left pnectomy	Empyema (Staph. aureus)	0	26	Neg.	Well. Empyema entirely closed with thoracoplasty
36	M. C.	34	F	1999	R. R.	10/29/42	II A	0	+	3½ years	0	Pnthx., thpl.	Rt. U. & M.	0	0	23	+	Has residual cavity in superior division of lower lobe
37	E. A.	33	F	1551	R. R.	10/30/42	III A	0	+	3 years	0	0	Left pnectomy	0	0	16	Neg.	Well
38	C. B.	22	M	1878	D. R.	12/ 1/42	III A	0	+	1½ years	0	Phrenic, pnthx.	Rt. pnectomy	0	0	22	Neg.	Well
39	J. T.	34	M	2269	R. R.	12/11/42	III B	+	+	7 weeks	0	0	Rt. pnectomy	0	Stump ulceration	24	Neg.	Well
40	T. B.	24	F	1903	R. R.	12/31/42	II A	0	+	22 months	0	Pnthx., thpl.	L. U. L.	Contralateral spread	—	—	—	Died on 5th p.o. day of contralateral pneumonia (? tuberculosis)
41	E. H.	38	M	2309	R. R.	1/12/43	III A	0	+	13 months	0	Pnthx.	Left pnectomy	Contralateral spread, tuberculosis of chest wall	0	22	Neg.	Well. Spread entirely healed. Incision healed by primary intention
42	E. C.	53	M	2260	R. R.	1/14/43	III A	0	+	1 year	0	0	Left pnectomy	0	0	21	Neg.	Well
43	M. P.	20	F	1655	R. R.	2/12/43	IV	0	+	20 months	0	Phrenic	L. U. L.	0	0	17	Neg.	Well
44	E. P.	39	F	830	R. R.	2/18/43	II A	0	+	5 years	0	Phrenic, thpl., revision	Left pnectomy	0	0	18	+	Clinically well. Slight cough and expectoration
45	P. G.	34	F	2384	R. R.	2/26/43	III A	0	+	9 months	0	0	Rt. pnectomy	0	0	14	Neg.	Well
46	I. M.	24	F	2421	R. R.	3/20/43	III A	0	+	7 months	0	Pnthx.	Left pnectomy	Tuberculosis of chest wall	0	23	Neg.	Well
47	J. C.	54	M	2385	D. R.	3/29/43	III B	+	+	4 years	0	0	Left pnectomy	Exacerbation of contralateral disease	—	32	—	Died on 53rd p.o. day of tuberculosis and pulmonary insufficiency
48	S. A.	25	F	2422	D. R.	4/ 2/43	III A	0	+	5 months	0	0	Left pnectomy	Paroxysmal irregular heart action	—	—	—	Died on 1st p.o. day
49	J. G.	31	F	1187	D. R.	4/15/43	III A	0	+	3½ years	0	R. L. L., phrenic	Rt. U. & M.	Contralateral spread	0	24	+	Has progressive tuberculosis
50	E. M.	44	F	2010	D. R.	4/16/43	II B	+	+	5 years	0	Phrenic, thpl.	Left pnectomy	0	Stump ulceration	37	+	Clinically well. Slight cough and expectoration

TABLE 8—*Continued*

	NAME	AGE	SEX	CASE NUMBER	PREOPERATIVE CLASSIFICATION	DATE OF OPERATION	INDICATION	ENDOBRONCHIAL TUBERCULOSIS	SPUTUM	DURATION OF DISEASE	PREVIOUS THERAPY: Contralateral lung	PREVIOUS THERAPY: Ipsolateral lung	OPERATION PERFORMED	COMPLICATIONS: Postoperative	COMPLICATIONS: Late	POSTOPERATIVE HOSPITAL DAYS	SPUTUM AT PRESENT	PRESENT CLINICAL STATUS
51	W. K.	22	M	2374	R. R.	3/22/43	IV	0	0	10 years	Pnthx.	0	L. U. L.	Temporary fistula closed with muscle transpl.	0	21	Neg.	Well
52	M. A.	34	F	1439	R. R.	4/26/43	V	0	0	3 years	0	Phrenic, pnthx.	R. L. L.	0	0	17	Neg.	Well
53	I. H.	22	F	1982	R. R.	4/27/43	II A	0	+	5¾ years	0	Thpl.	L. U. L.	0	0	16	+	Clinically well
54	M. M.	32	F	2402	D. R.	5/ 3/43	III B	+	+	2½ years	Phrenic	Pnthx.	Rt. pnectomy	Circulatory collapse	0	—	—	Died on 2nd p.o. day
55	C. P.	25	F	1470	R. R.	5/ 7/43	IV	0	+	5½ years	0	Pnthx.	R. U. L.	0	0	10	Neg.	Well
56	M. D.	33	F	914	R. R.	5/20/43	V	0	+	6 years	0	Phrenic	L. L. L.	0	0	12	+	Clinically well
57	M. C.	25	M	2052	R. R.	6/ 4/43	II A	0	+	2 years	0	Pnthx., thpl., revision	Left pnectomy	0	0	19	Neg.	Well
58	A. C.	21	F	2502	R. R.	6/ 1/43	III B	+	+	7 months	0	Pnthx.	Left pnectomy	0	Developed fistula and mixed empyema, Feb. 1944	20	+	Has fistula and mixed tuberculous empyema
59	M. K.	28	F	2513	R. R.	6/ 7/43	IV	0	+	2¼ years	0	0	Left pnectomy	Tuberculosis of chest wall	0	16	Neg.	Well
60	L. W.	25	F	2565	D. R.	6/12/43	III B	+	+	6 months	0	0	Rt. pnectomy	Stump ulceration, contralateral spread	0	16	Neg.	Well. Stump healed with $AgNO_3$ treatment
61	G. T.	35	F	2032	R. R.	6/21/43	III B	+	+	3½ years	0	Pnthx.	Left pnectomy	Empyema (Staph. aureus)	0	16	Neg.	Well
62	M. S.	34	F	2489	R. R.	6/15/43	II A	0	+	9 years	0	Phrenic, thpl.	L. U. L.	0	0	0	Neg.	Well
63	A. B.	39	F	2568	R. R.	7/ 1/43	III B	+	+	11 years	0	Pnthx.	Rt. pnectomy	Embolism	—	—	—	Sudden death on 15th p.o. day

64	G. D.	53	M	2240	R. R.	8/26/43	III B	+	+	23 months	0	Phrenic	Rt. pnectomy	? contralateral exacerbation	0	22	+	Clinically well
65	M. P.	38	F	2647	D. R.	9/ 2/43	III B	+	+	16 months	0	Pnthx.	Left pnectomy	0	0	8	Neg.	Well
66	L. B.	27	F	2232	R. R.	9/20/43	III A		+	15 months	0	Pnthx.	Rt. pnectomy	0	0	10	Neg.	Well
67	P. P.	32	F	2642	R. R.	9/21/43	III B	+	+	5 years	0	Pnthx.	Left pnectomy	Contralateral spread	0	17	+	Slight cough and expectoration
68	R. B.	37	M	2702	R. R.	10/ 1/43	IV	0	+	16 months	0	Pnthx.	R. U. L.	0	0	14	Neg.	Well
69	D. N.	31	F	2701	R. R.	10/ 7/43	V	0	+	14 months	0	0	Left pnectomy	0	0	11	Neg.	Well
70	L. B.	23	F	2718	R. R.	10/11/43	III A	0	+	8 months	0	Pnthx.	Rt. pnectomy	0	0	12	Neg.	Well
71	M. F.	49	F	2716	R. R.	10/21/43	IV	0	+	15 years	0	0	R. U. L.	0	0	11	?	Well
72	M. F.	30	F	1731	D. R.	10/23/43	III B	+	+	3 years	0	Pnthx., thpl.	Rt. pnectomy	Postoperative shock	—	—	—	Died few hours after operation
73	J. G.	49	M	1757	D. R.	10/25/43	II B	+	+	19 years	0	Thpl.	Rt. pnectomy	Pulmonary insufficiency	—	—	—	Died on 19th p.o. day
74	E. J.	22	F	2736	R. R.	10/29/43	IV	0	+	11 months	0	Phrenic	R. U. L.	0	Progressive disease in rt. M. & L. lobes	15	?	Clinically well. X-ray shows spreading lesion
75	E. C.	23	F	2726	R. R.	11/ 3/43	III B	+	+	13 months	0	Pnthx.	Left pnectomy	Contralateral spread	0	20	+	Progressive tuberculosis
76	J. C.	35	M	2026	R. R.	11/16/43	III A	0	0	20 months	0	Pnthx.	Rt. pnectomy	0	0	18	Neg.	Still forming some fluid in rt. pleural space. Clinically well
77	M. L.	24	F	2488	D. R.	12/10/43		0	+	20 months	Pnthx.	Pnthx.	R. U. L.	Cavity in apex of L. L. L.	0	10	+	Had L. U. lobectomy 2 months later
78	A. A.	35	F	2399	R. R.	12/27/43	III B	+	+	18 months	0	Phrenic, pnthx.	Left pnectomy	0	0	10	Neg.	Well

Of the 13 desperate risks, 5, or 45.4 per cent, are clinically well and have negative sputa. Of these 5, 3 have been discharged from the sanatorium and are now leading normal, active lives. One is at home on bed-rest. The other is still in the sanatorium and is now on graded activity. The fact that 45 per cent of these patients have been salvaged seems to justify the acceptance of at least some of these desperate risks for resection.

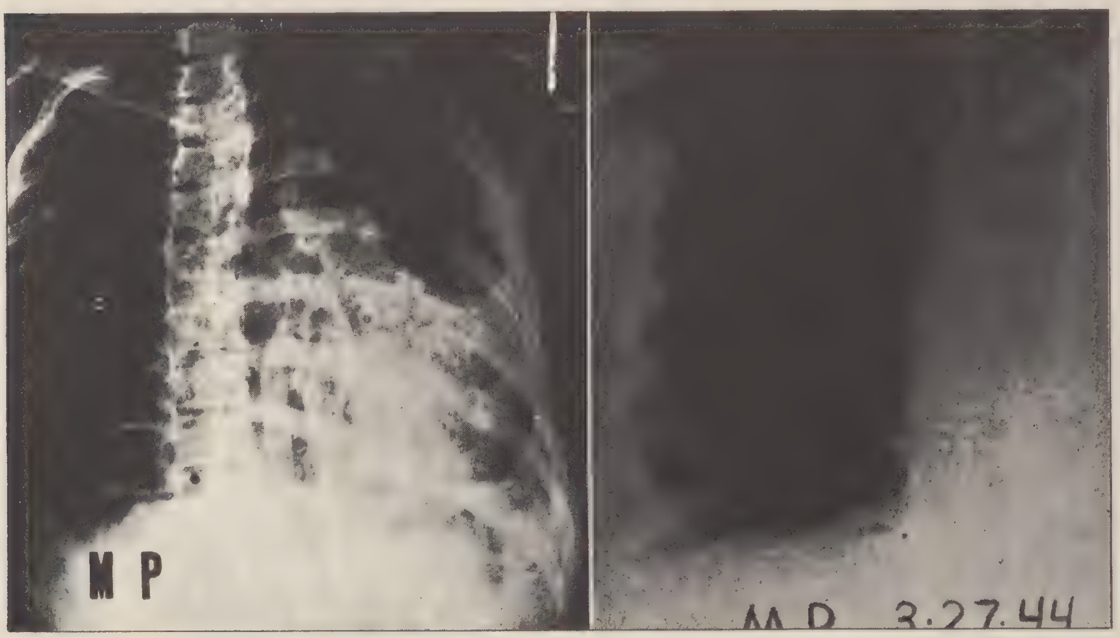


FIGURE 3A

Mrs. M. P. Age thirty-eight. Case #65 in table 8. Patient had been ill for sixteen months, during which time she had become progressively worse. Bronchoscopy revealed an ulcero-stenosis involving the left upper and lower lobe bronchi and the adjacent portion of the main bronchus. Patient was toxemic and had low grade fever. An unstable lesion was present in the contralateral lung. She was classified preoperatively as a desperate risk. Left penumonectomy was performed on September 2, 1943. Since then the patient has been asymptomatic. Her sputum is consistently negative or seventy-two hour concentrates.

Left: Roentgenogram just prior to resection showing a huge cavity in the left upper lobe and extensive involvement of the entire left lung. Note the nodular infiltration in the right lung in the second and third interspaces.

Right: Roentgenogram on May 3, 1944 showing post-pneumonectomy and post-thoracoplasty state. A lateral type of thoracoplasty was performed six weeks after pneumonectomy to prevent mediastinal distortion and emphysema of remaining lung. This was accomplished in one stage and without removing the first rib or transverse processes. Note absence of scoliosis.

Five of these patients have died during the postoperative period. The remaining 3 will eventually die of tuberculosis.

The justification for the separation of statistics lies in the fact that none of the desperate risks would have been accepted for thoracoplasty in the vast majority of thoracic clinics. Thus, the statistics of the reasonable risks offer a series of cases in which the results may be compared with those of the various collapse therapy reports.

The evaluation of the condition of the contralateral lung is a matter of great importance when pulmonary resection is contemplated in the tuberculous patient. Naturally, the criteria in respect to a contralateral lesion must be more rigid when pneumonectomy is anticipated than when lobectomy is to be performed.

FIGURE 3B

Surgical specimen (left lung) demonstrates the huge cavity in the left upper lobe and the extensive involvement of the entire lung by caseous foci. The bronchi were extensively involved. The following is the pathological report: "Cut surface shows a diffuse scattering of yellow-gray nodules throughout both lobes, but expecially in the lower lobe about equal in dorsal and inferior portions. The majority of the upper lobe, except anterior portion, is occupied by an irregular cavity 8 x 4 x 4 cm. which is in direct communication with a main branch of the upper lobe bronchus near its origin. All bronchi show granular mucosa and thickened walls. The main stem bronchus shows marked narrowing of its lumen down to about 0.3 x 0.5 cm. Hilar nodes are enlarged and contain many gray nodules."

Following pneumonectomy, bed-rest alone must be relied upon to control the remaining lesion. In reference to lobectomy, contralateral pneumothorax or temporary phrenic paralysis may be employed either before or after the resection. When pneumonectomy is to be performed, the contralateral lung must not harbor an uncontrolled lesion or one that is deemed uncontrollable. However, we do not agree with those who maintain that the contralateral lung must be absolutely free of involvement. Of the 59 patients in this report, 22 had

contralateral lesions. The extent of the contralateral lesion was considered to be minimal in 16. Two of these patients previously had had extensive involvement of the contralateral lung, which had cleared quite markedly and left behind

FIGURE 3C

Photographs of Mrs. M. P. (See figures 3A and 3B.) Case #65 in table 8. Note absence of deformity, particularly position of shoulder girdle and lack of cervical or thoracic scoliosis.

a minimal inactive lesion. Another patient had had an evanescent minimal lesion three months prior to resection. This had entirely cleared by the time pneumonectomy was performed. Three patients had moderately advanced lesions in the contralateral lung. One patient had a contralateral pneumothorax at the time left upper lobectomy was performed. The remaining patient was one who had bilateral upper lobe giant cavities. A program of bilateral upper lobectomy was planned and recently has been completed. Contralateral lesions were considered to be unstable in 5 and inactive in the remaining 17 patients. Of these 22 patients with contralateral disease, 16 were treated by pneumonectomy and 6 by lobectomy.

The follow-up of these patients has shown that 18 of them have had no contralateral exacerbation. This includes 3 patients whose contralateral lesions preoperatively were considered to be unstable. The following is a description of the remaining 4 patients:

1: A fifteen-year-old female was treated with right pneumonectomy. Three months before the operation this girl had an evanescent exudative lesion in the extreme left apex which had entirely cleared at the time resection was performed. This patient remained well and negative for eighteen months. At this time she developed an acute tuberculous pneumonia in her left upper lobe which was rapidly progressive and caused death within four weeks.

2: A thirty-nine-year-old white female was treated by left pneumonectomy. Preoperatively the X-ray films revealed a very small inactive infiltration far out in the third interspace in the right lung. She was completely well for the first eight months and the X-ray films during this time revealed no contralateral spread. Eight months following resection, however, the X-ray films showed a new lesion developing just adjacent to the previous involvement. This progressed for the first two months and since then has been retrogressive. at the present time it is a fairly stationary lesion. This patient is consistently negative on all tests, including examination of the concentrated sputum, of the bronchoscopically aspirated specimen and the gastric specimen.

3: A fifty-four-year-old white male in extremely poor general condition who had been quite ill for four weeks prior to operation and was still running fever at the time resection was performed. He had a marked fibrous stenosis at the orifice of the left main bronchus, with total destruction of the left lung by tuberculosis and an associated anaerobic infection. He had a minimal lesion in the right apex and first interspace and, during the week prior to resection, developed râles over the right lower lobe and suggestive infiltration at the base. He was classified as a desperate risk and resection was performed; it was realized that this offered him his only chance to live. This patient had a slowly progressive contralateral lesion during the first four weeks postoperatively; it then spread more rapidly, and on the fifty-third day he died of infection and pulmonary insufficiency.

4. A fifty-three-year-old white male was treated by right pneumonectomy. Preoperatively, he had a minimal lesion in the second interspace on the left side. Postoperatively, this lesion appeared to have fuzzier edges and was less well defined. Although it never increased in extent, it has been classified as a questionable contralateral exacerbation because of the change in appearance. Since that time this lesion has become quite fibrotic in appearance. The patient is clinically well and has a negative sputum on concentration.

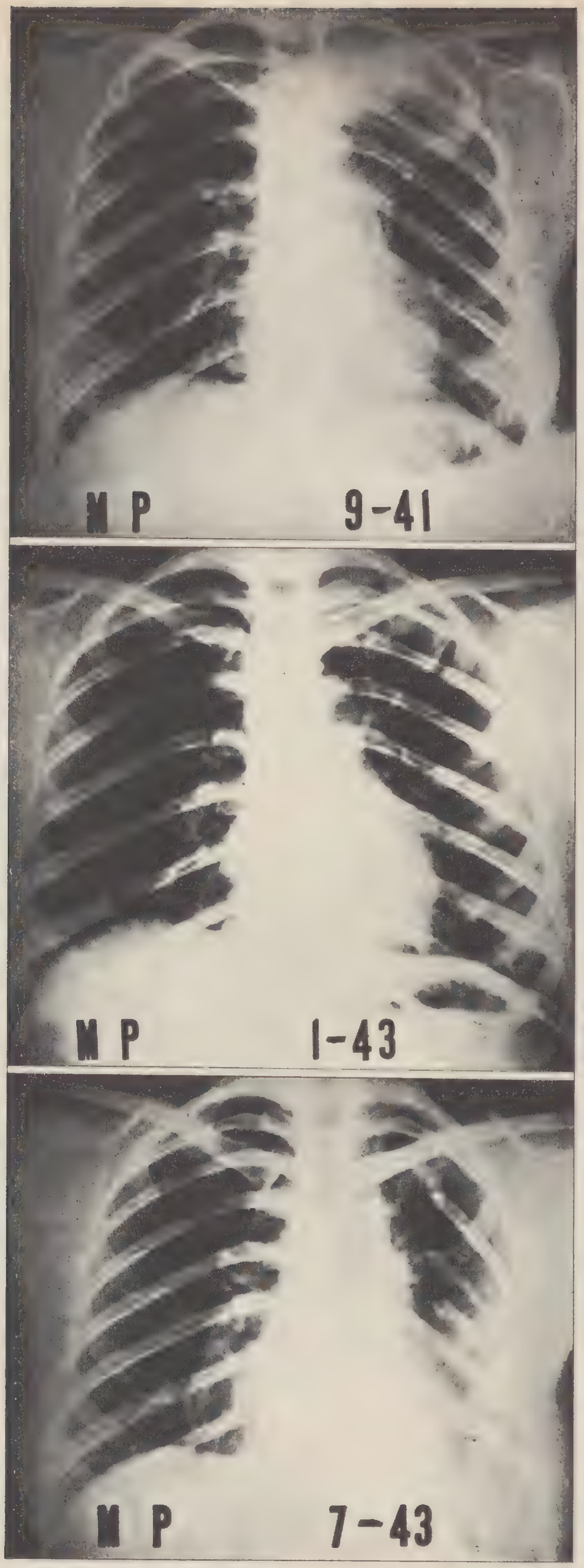


FIGURE 4A

FIGURE 4A

Miss M. P. Age twenty. Refer to case #43 in table 8 for details.

Upper: Roentgenogram in September, 1941, showing an active exudative lesion in the left upper lobe with a 2 cm. cavity in the first interspace.

Centre: Roentgenogram in January, 1943, after sixteen months of bed-rest and phrenic paralysis. There has been definite clearing, but a dense homogeneous lesion with residual cavity remains at the apex. Sputum positive.

Lower: Roentgenogram in July, 1943, five months following left upper lobectomy. There is no evidence of residual parenchymal disease.

Note: Resection in this case was an elective operation. It was performed in preference to thoracoplasty or a trial of pneumothorax. Her sputum has been consistently negative on all tests including guinea pig inoculation. She is asymptomatic and has returned to normal activities.

FIGURE 4B

Surgical specimen (left upper lobe) showing the extensive involvement of the apex with a residual slit-like cavity filled with caseous material. The following is the pathological report: "On cut section apical half of lobe contains numerous yellow nodules varying from few mm. up to 0.5 cm. in diameter. These are surrounded by thin gray membrane. Only occasional similar nodule found in lower half. Remainder of lung tissue atelectatic. Also in upper half there is a collapsed cavity 3.5 x 0.5 cm. filled with yellow caseous material."

In summary, it can be said that 18 of the 22 patients who had contralateral lesions prior to resection have had no indication of contralateral exacerbation. Two patients have died as a result of contralateral exacerbation; one in the postoperative period and one eighteen months following resection. The remaining 2 patients who had contralateral exacerbation, as described above, are clinically well and have consistently negative sputa.

POSTOPERATIVE SPREADS

As stated earlier in this paper, postoperative spread remains the greatest threat to the tuberculous patient coming to pulmonary resection. It occurred in 7 patients, or 11.6 per cent of the present series. The fate of these 7 patients was as follows: One patient died on the fifth postoperative day of a contralateral tuberculous pneumonia. Two patients have progressive contralateral disease; at the present time both these patients have positive sputum. One has a receding contralateral lesion and a small cavity. This patient likewise has a positive sputum (Gaffky IV). Another has had marked clearing of the contralateral lesion; this has been stationary now for many months. This patient has a consistently negative sputum on all tests, including examination of the gastric specimen and guinea pig inoculation. The contralateral spread in the remaining 2 patients followed a very interesting and unusual course. Both had considerable spread on the first postoperative film taken within three days following resection. In one, this had entirely cleared within three weeks and, in the other, within six weeks. Both of them are well and their sputa are consistently negative on all tests, including guinea pig inoculation.

As the previous table on complications has shown, the incidence of contralateral spread is almost the same for those treated by pneumonectomy as for those treated by lobectomy. In our opinion, postoperative spread is due to bronchial spilling at the time of operation and is in no way related to the type of operation performed. It is most likely to occur in those who have large amounts of secretion at the time of resection.

In summary, it can be said that postoperative spread has occurred in 11.6 per cent of the patients. It has caused postoperative death of one and will eventually cause the death of 3 more. The prognosis of the remaining 3 appears to be good.

THE PROBLEM OF POSITIVE PLEURAL FLUID

Three patients have been accepted for resection who had pneumothorax complicated by pleural fluid in which tubercle bacilli were demonstrated by guinea pig inoculation. Two of them also had tuberculous bronchitis. One patient following resection developed an empyema caused by *Staphylococcus aureus*. At the time the empyema was drained, pleural fluid was collected for study and biopsy of the pleura was taken. The biopsy revealed no evidence of tuberculosis, and the pus from the pleural cavity was negative for tubercle bacilli on concentration and guinea pig inoculation. A thoracoplasty has since been performed on this patient to obliterate the empyema space, and she is clinically well at the

present time. The second patient's convalescence was uneventful. She was clinically well and her sputum was negative for nine months following the resection, at which time she developed a bronchial fistula and a tuberculous empyema. The empyema was drained, and at the present time the bronchial fistula is being treated by cauterization with sodium hydroxide. The third case is clinically well and has a consistently negative sputum. However, he has continued to form a small amount of fluid since the time of resection and has required several thoracenteses. On one occasion the pleural fluid was found to be positive. On all other examinations it has been negative. This patient has not required a pleural tap for the past six weeks, and at present there is no evidence of accumulation of fluid. The presence of a positive pleural fluid is certainly an additional hazard, but should not be considered in itself a contraindication to resection. All 3 of these patients described were treated by pneumonectomy.

EXTENT OF RESECTION

The amount of lung tissue to be resected is a matter of prime importance. It depends on two main factors: (*1*) the extent of the parenchymal disease, and (*2*) the presence of bronchial disease. It must be remembered that pulmonary resection is being performed to remove all disseminating foci of tuberculosis. It is not sufficient to remove the most evident offending lesion and leave behind less extensive, but nevertheless potentially dangerous, foci of infection. The complete conversion of the sputum is a prerequisite of success in this form of treatment of tuberculosis, as it is in all other forms of therapy. Our experience to date has shown that the resection of too little, and not too much, pulmonary tissue may be responsible for an unsatisfactory result.

When the main bronchus or the orifice of one of the lobar bronchi is involved with tuberculous bronchitis, pneumonectomy can be decided upon prior to operation, as it is absolutely essential to remove these foci. Frequently, however, the extent of resection cannot be finally decided upon until the chest is opened and the lung palpated. It is difficult to determine by palpation whether or not a lesion is active, and one must rely more upon the extent of the disease. Not infrequently considerable involvement is found in one of the lobes in which it was not suspected by X-ray study. The superior division of the lower lobe is notorious in this respect.

From a purely technical standpoint, it is usually possible to perform lobectomy if this is desirable. In only 2 instances have we found the tuberculous involvement extending directly across the fissure line so that lobectomy was impossible. In such cases one is faced with the possibility of doing either a pneumonectomy or a segmental type of lobectomy. At times, in the presence of an undeveloped fissure on the right, we have elected to do a double lobectomy (that is, upper and middle or lower and middle) rather than develop the fissure line by cutting across pulmonary tissue.

Pathological study of the surgical specimens has revealed that, almost without exception, there is extensive involvement of the superior division bronchus when a cavity is present in this segment of the lower lobe. Frequently this involve-

ment extends throughout the course of the bronchus, and the adjacent main bronchus is involved with a submucosal or more advanced type of tuberculosis. In such cases, regardless of bronchoscopic findings, the presence of a marked tuberculous bronchitis of the superior division bronchus must be assumed. This presents a hazard to lower lobectomy in such cases. On the right side, it would seem more advisable to perform a right middle and lower lobectomy, so that the suture line through the bronchus can be placed at a higher level, and increase the chances of getting above the disease.

THE PROBLEM OF ACTIVE DISEASE IN THE LUNG TO BE RESECTED

The presence of active, spreading disease in the lung to be resected is not a contraindication to resection. In fact, it frequently is the indication for resection. We do not agree with those who claim that the patient must have established a so-called immunological balance before operation is performed. This concept has deprived many patients of their only chance to get well, as often many of them continue to progress and fail to establish the immunological balance at any time. Complications, such as empyema, bronchial fistula and implantation of the infection in the incision, have not been encountered more frequently in such patients, as was suggested by Churchill and Klopstock (2). Contrary to this, we have found tuberculous granulation tissue in the chest wall of only 3 patients. All 3 had been on sanatorium regimen for many months, and 2 of them had been treated by pneumothorax.

TECHNICAL CONSIDERATIONS

Resection of lung tissue involved with tuberculosis is dispatched with greater ease than any other group of patients coming to pulmonary resection. To date, no tuberculous patient has come to resection in whom the operation was not technically possible. Regardless of how adherent the costal pleura may be, as soon as this portion is mobilized the mediastinal surface is usually found to be relatively free, and the lack of adhesions and induration is quite remarkable. Hilar lymph nodes are usually small, the tissue planes are well preserved and the marked fixation of the hilar structures commonly associated with suppuration and tumor is rarely seen.

Individual ligation of the hilar structures is always used. In our opinion, the tourniquet is an instrument which should never be used by the surgeon performing resection for tuberculosis. Individual ligation technique can be applied to either lung or to any of the various lobes, including the left upper lobe. The individual ligation of the hilar structures of the left upper lobe offers no unusual technical difficulties.

The bronchus is closed with silk sutures. When technically feasible, only end-sutures are used. When additional support is desired, a row of mattress sutures is used also. A pleural flap is then developed from the posterior chest wall and reflected over the bronchus. It is sutured into the end of the bronchus.

The meticulous and atraumatic handling of pulmonary tissue, particularly that part which is to remain in the case of segmental resection or lobectomy, is

an important technical consideration. Individual ligation of the hilar structures and the pleural flap method of closing the bronchus are the key notes to success in resection of tuberculous lung tissue.

THE PROBLEM OF ENDOBRONCHIAL TUBERCULOSIS

The evaluation of the condition of the bronchial tree is of utmost importance prior to resection in all tuberculous lungs. An endobronchial lesion, either active or inactive, has not been considered a contraindication to resection. On the contrary, it has often been considered as an indication for resection. It must be considered in determining the extent of the pulmonary resection, as ideally both the parenchymal and the bronchial foci should be removed.

Nineteen, or 31.7 per cent of this resection series, had bronchial lesions visible through the bronchoscope. These were classified as follows: submucosal involvement in one, ulceration in 5, ulcero-stenosis in 9 and fibrostenosis in 4. These bronchial lesions were distributed as follows: 4 involved the right upper lobe orifice, one the right main bronchus, 2 the right intermediate bronchus and one the right upper and right intermediate bronchus, 10 the left main bronchus and one the left upper lobe orifice.

The position of the bronchial suture line with reference to the preëxisting bronchial lesion is a matter of interest and importance. Judged by bronchoscopy, the suture line was above the bronchial lesion in 5, immediately adjacent to it in 10 and below it in 4.

Thirty-five patients have been bronchoscoped since operation. Five have been found to have ulceration in the bronchial stump. Four of these patients were treated by pneumonectomy and one by a right lower lobectomy. The incidence in patients bronchoscoped is 14.3 per cent, and for the entire series of 60 patients is 8.3 per cent. In all 5 of the patients who developed ulceration of the bronchial stump, the bronchial suture line had to be placed in or immediately adjacent to an active bronchial lesion. The stump ulcers have been treated, as previously stated, by application of 30 per cent silver nitrate at two-week intervals. Three have been controlled and one patient still has ulceration with positive sputum, but she has failed to return for regular treatment. The remaining patient who had an ulceration of the stump of the right lower lobe bronchus has been treated by further resection. Her bronchial lesion failed to respond to local therapy.

During the past year Dr. William Meissner (4) has studied the problem of endobronchial tuberculosis in the surgical specimens submitted to him following resection. This has been a painstaking piece of work, and has been performed in the following manner: at the time of resection a small segment of the main bronchus is reamputated to provide tissue for study. Then, from the surgical specimen, sections are taken from the remaining portion of the main bronchus, from each of the lobar bronchi, and from each of the segmental bronchi of the various lobes. This study has revealed that tuberculous bronchitis originates in the small bronchi draining the parenchymal foci, extends toward and may eventually involve the main bronchus. Thus, in all cases where involvement

of the main bronchus is found, lobar and segmental bronchi have likewise been found to be involved. Unfortunately, 6 of the small bronchial segments which were taken immediately adjacent to the suture line were lost. Of the remaining 30 pneumonectomy specimens examined, 15, or 50 per cent, revealed tuberculous involvement. The main bronchus was involved in 20, or 56 per cent, of the 36 pneumonectomy specimens. Of the 24 lobes examined, 4 showed tuberculous involvement of the lobar bronchi. Forty-three of the 60 specimens showed involvement of the segmental bronchi. This is an incidence of 71.6 per cent. It is of interest to note that only 12, or 50 per cent, of the 24 lobes showed segmental involvement, whereas 31, or 86.1 per cent, of the 36 pneumonectomy specimens showed involvement of the segmental bronchi. This would indicate the greater severity of the disease in those treated by pneumonectomy. Such a high incidence of bronchial involvement would seem to indicate that the tuberculous involvement of the segmental bronchi is almost universally associated with parenchymal tuberculosis.

The importance of this pathological study is quite evident. It indicates that the main bronchus is involved much more frequently than has ever been suspected by bronchoscopy. It also establishes the fact that bronchial sutures have been placed in involved tissue in many instances. In spite of this, ulceration has occurred only in 5 cases. The important clinical fact is that the bronchial closure remains intact in spite of the presence of tuberculous bronchitis. This has been demonstrated since there has been only one fistula in this entire series of cases. It is true even in those who developed ulceration in the stump. None of these 5 patients developed fistula.

RESECTION AS PREFERRED TREATMENT

In a previous paper (5) the types of disease in which resection should receive preferential consideration were outlined. The following quotations from that paper also represent our convictions to-day.

"Although it may be unwise to outline specific indications for an operation which has evoked so much controversy, our experiences prompt us to consider resection as the treatment of choice for the following types of disease:

1: In preference to thoracoplasty in cases with active parenchymal disease complicated by bronchial stenosis.
2: Extensive basal tuberculosis with or without associated bronchiectasis.
3: In unilateral disease that has failed to respond to a pneumothorax with apparently adequate collapse.
4: In unilateral disease that has failed to respond to an adequate thoracoplasty.
5: In preference to cavernostomy in the treatment of tension cavities in unilobar or extensive unilateral disease.
6: In extensive unilobar disease with dense opacities and little evidence of fibrosis and retraction.
7: Progressive unilobar or unilateral tuberculosis in the teen-age group.
8: Tuberculoma."

CONCLUSION

Pulmonary resection is an effective and reasonably safe form of treatment for tuberculosis in patients in good general condition. It also salvages some of the desperate risks who otherwise face an imminently fatal issue. The present results have been obtained in spite of the fact that the vast majority of patients accepted for resection have been those with extensive or complicated forms of tuberculosis.

In our opinion, pulmonary resection will be applied in the future to more patients and will find its true place as a supplementary and not a competitive form of treatment to the already established methods of rest and collapse therapy. It will undoubtedly become an elective procedure in certain types of disease. It will also find a widening field of usefulness in the complicated forms of tuberculosis in which collapse therapy has been found to be relatively ineffective or dangerous.

Any report on pulmonary resection as a form of treatment for tuberculosis must be considered as a preliminary report at this state of our knowledge and experience. Because of the nature of the disease being treated, time and rigid follow-up of these patients will eventually tell the true story.

However, enough experience has already been gathered to show that many of the complications and failures in the past have been due, not to tuberculosis *per se*, but to improper technique, the poor selection of patients and, in many instances, to the removal of too little lung tissue. Although the preservation of function is an ideal to strive for and is frequently attained by resection, there are times when tuberculosis, like cancer, must be extirpated at the sacrifice of some functional lung tissue.

The addition of pulmonary resection to our armamentarium in the treatment of tuberculosis places an even greater challenge before clinicians. It is now more important than ever to recognize certain patterns of tuberculosis that respond best to certain types of therapy and fail to respond to others. Only in this way can we apply the proper treatment and avoid serious complications. The old trial and error method of treating pulmonary tuberculosis is no longer justifiable. Complication and failure of other methods should be anticipated on the basis of experience and proved clinical observation.

Pulmonary resection should be used not as a last resort, but before extension of disease and complications have occurred. The earlier it is performed, the greater the possibility of conservation of pulmonary function and the greater the chance of cure.

SUMMARY

1. Results have been presented for 60 consecutive pulmonary resections for tuberculosis performed between January 1, 1942 and January 1, 1944. There were 36 pneumonectomies and 24 lobectomies.

2. Resection of the tuberculous lung usually is accomplished with greater ease than in cases of pulmonary suppuration or malignancy.

3. Individual ligation of the hilar structures and the meticulous closure of the bronchus with silk sutures and a reinforcing pleural flap have almost eliminated bronchial fistula and empyema as complications.

4. Contralateral spread remains the greatest hazard in pulmonary resection for tuberculosis.

5. Ulceration of the bronchial stump occurred in 8.5 per cent of the patients. This can be diagnosed only by routine bronchoscopy following resection. It may occur early or late in the postoperative period.

6. Active tuberculosis in the lung to be removed is not a contraindication to resection. Waiting for stabilization of the lesion frequently robs these patients of their only chance to get well.

7. Tuberculous bronchitis, either active or inactive, is not within itself a contraindication to resection. It is often an indication for resection.

8. A contralateral lesion is not a contraindication to resection unless it is uncontrolled or uncontrollable.

9. The total operative fatality is 11.6 per cent. The operative fatality in the 47 "reasonable risk" cases is 4.3 per cent and in the 13 "desperate risk" cases is 38.5 per cent.

10. When the patient is in good general condition, the operative fatality for lobectomy and pneumonectomy is almost identical.

11. Pulmonary resection should be considered as a possible method of treatment in outlining therapy for tuberculous patients. Ideally it should be applied before extension of disease and complications occur.

REFERENCES

(1) Alexander, John: The Collapse Therapy of Pulmonary Tuberculosis, 1937, Charles C. Thomas, Publisher.

(2) Churchill, E. D., and Klopstock, Robert: Lobectomy for pulmonary tuberculosis, Ann. Surg., 1943, *117*, 641.

(3) Kent, D. M., and Blades, Brian: The surgical anatomy at the pulmonary lobes, J. Thoracic Surg., 1942, *12*, 18.

(4) Meissner, William: Personal communication.

(5) Overholt, R. H., and Wilson, N. J.: Pulmonary resection in the treatment of tuberculosis, (submitted for publication).

(6) Thornton, T. F., Jr., and Adams, W. E.: The resection of lung tissue for pulmonary tuberculosis, Surg., Gynec. & Obst., 1942, *75*, 312.

DISCUSSION

Dr. Henry D. Chadwick, Waltham, Massachusetts: I have had the opportunity to read Doctor Overholt's paper and I have seen several of the patients included in this series. His analysis of the results shows that the hazards of empyema and bronchial fistula have been largely overcome and the operative mortality reduced to a degree that gives pulmonary resection a standing as a method of treatment of advanced pulmonary tuberculosis that we clinicians should welcome as a means of saving some otherwise hopeless cases.

The advances made in operative technique, in anesthesia and in chemotherapy have made lobectomy and pneumonectomy so much safer that, when other methods fail to control the disease, we should not hesitate to recommend them.

Instead of stressing the mortality from pulmonary resection, we should keep in our minds that, out of 60 pulmonary resections, 53 were successfully performed; that, out of 46 patients classed as reasonable risks, only 3 were unsuccessful and, of these, 32 have a good prognosis and negative sputum, 9 others a guarded prognosis and only 3 are listed as in poor condition.

These cases have had what might be called standard methods of treatment and some of them were in sanatoria for years and the resections were done only as a last resort. Under these circumstances, this high salvage rate is a credit to the operator and gives us another offensive weapon to use in the treatment of pulmonary tuberculosis.

The patients we should refer to the thoracic surgeon for resection are the following types:

First, those with bronchial tuberculosis with stenosis which makes pneumothorax or thoracoplasty inadvisable.

Second, cases with thick-wall and tension cavities that cannot be collapsed by pneumothorax or thoracoplasty.

Third, patients in whom thoracoplasty has been performed, but who continue to raise positive sputum and in whom bronchoscopic examinations and X-ray studies make it reasonably certain that the bacilli come from the operated side.

Fourth, patients with extensive, productive disease, with or without bronchiectasis, especially basal lesions.

Preferably, the above cases should be unilateral, but, even if there has been some slight involvement of the contralateral lung and the disease is retrogressive or stable, resections are not contraindicated.

The danger of contralateral spreads remains a menace and occurred in 12 per cent of Doctor Overholt's cases. We know, however, that such spreads frequently occur in advanced pulmonary tuberculosis after thoracoplasty, pneumothorax or when only bedrest is carried out. Therefore, this possibility should not deter us from an operative procedure when it is indicated.

It is important, it seems to me, that a resection, either a lobectomy or a pneumonectomy, should be followed by a modified thoracoplasty to obliterate the space left by the resection. Otherwise, in lobectomy, overexpansion of the remaining lobes, if they contain tuberculous foci, might cause activation of the disease and, in pneumonectomy, emphysema of the remaining lung would occur that would decrease the respiratory reserve if this precautionary measure were not taken.

Dr. J. Maxwell Chamberlain, Cooperstown, New York: My discussion will be limited to one phase of this problem: namely, upper lobectomy.

When disease is limited to the upper lobe and conservative measures have failed, we frequently resort to two forms of therapy: a selective thoracoplasty or an upper lobectomy. In a report a few years ago Doctor Overholt found the modern selective thoracoplasty successful in converting the sputum in 90 per cent of the cases and the fatality rate in this series was less than 3 per cent. The operation was unsuccessful therefore in 7 per cent of the cases. Recently I reviewed 46 consecutive modern selective thoracoplasties with a partial scapulectomy for disease limited mainly to the upper lobe, and found that the operation converted the sputum in 80 per cent of the cases (concentrate examination). The fatality rate was less than 2 per cent. From these figures and others in the literature, it is safe to say, therefore, that the disease in an upper lobe will be controlled (from a pathological point of view) in from 80 to 90 per cent of cases and the few failures can still have a lobectomy with probably less risk, because after a thoracoplasty the sputum con-

tains fewer organisms, is diminished in amount and, should an empyema occur, the pleural space is reduced in size and the problem simplified.

Consideration must also be given to the pulmonary dynamics subsequent to either of these procedures, since little has been gained by a bacteriological cure if the patient becomes a respiratory cripple. Physiologists teach us that the diaphragm and lower six ribs are mainly responsible for the ventilatory burden, while the upper lobes contribute comparatively little. The loss of function by a selective thoracoplasty may therefore not be great in an upper lobe already partially destroyed by disease. In 12 patients with selective six-rib thoracoplasties on whom bronchospirometric studies were done by Wright and Woodruff before and after operation, it was found that 3 patients showed a reduction in function, 6 patients showed no significant change and 3 patients showed improvement. In 25 per cent, then, there was some reduction in function and in 75 per cent there was no significant change. We know less about respiratory function after lobectomy but I should like to review 3 cases on whom Doctor Wright was good enough to do bronchospirometric studies.

First, may I show the functional studies on a typical six-rib selective thoracoplasty with a partial scapulectomy. His maximum minute ventilation is 89 liters, his vital capacity 2.5 liters, and his divided function shows that the right lung (thoracoplasty) is doing 47 per cent of the ventilation and the normal left lung 53 per cent. The oxygen consumption on the right is 40 per cent and on the left 60 per cent. In the next patient a mistaken diagnosis of a tuberculoma was made and an upper lobectomy was done without any postoperative complications. Functional studies one year after operation are not quite as good as those in the patient above, though the maximum minute ventilation and vital capacity are about the same, namely, 90 liters and 2.5 liters, respectively. The divided function shows that 40 per cent of the ventilation is being done by the left overdistended lower lobe while the right lung is doing 60 per cent, but the oxygen consumption on the left is only 30 per cent and on the right 70 per cent. The third case is one in which an apical empyema occurred after an upper lobectomy, but responded well to drainage. For six months the wound was healed, the patient was without symptoms and back to full-time work when she began to have pulmonary hemorrhage. Bronchoscopy revealed a kinked right stem bronchus from angulation of the lobe as it ascended into the thoracic vault and a small pea-sized granuloma which was removed with biopsy forceps several times before it completely disappeared. Gradually a shadow appeared at the apex of this overdistended lobe and the patient now has a small pulmonary abscess two years after lobectomy. The maximum minute ventilation is 65 liters, the vital capacity 1,500 cc. and the divided function shows that the minute ventilation on the right is 40 liters and on the left 60 liters; but the oxygen consumption on the right is only 10 per cent and the left is consuming 90 per cent. Ventilation is good but oxygen consumption is poor.

Therefore, if the function after upper lobectomy is not improved over that after a selective thoracoplasty (with a partial scapulectomy) and the rate of sputum conversion remains the same or is lower, it does not seem justifiable to do the more hazardous operation, namely, lobectomy as the initial procedure.

Dr. John Alexander, Ann Arbor, Michigan: At present, the following things seem of special importance with regard to pulmonary resection for tuberculosis:

(*1*) Both lobectomy and pneumonectomy have a definite place in the treatment of tuberculosis and have been used in a number of clinics for more than ten years for patients in whom no other form of therapy offered a reasonable chance of recovery.

(*2*) Great praise is due to Doctor Overholt and Doctor Wilson for their boldness and

the skill they have demonstrated in operating upon and saving certain of the patients whose cases they have just shown to us.

(*3*) The indications for thoracoplasty are broad and, in my opinion, those for lobectomy and pneumonectomy are narrow. During the last two years I have recommended lobectomy or pneumonectomy for only a small fraction of the number of patients Doctor Overholt has chosen.

(*4*) The early and late fatality rates and the percentage of postoperative complications in the modern type of thoracoplasty are very low and the percentage of apparent cures is high, even when thoracoplasty is routinely used for many of the lesions which Doctor Overholt believes should be treated by pneumonectomy or lobectomy.

(*5*) Except for Doctor Maier's remarkable record of only one death (6.2 per cent) among his 16 pneumonectomy and lobectomy patients, I know of no series of cases as large as his in which the early fatality rate is less than Doctor Overholt's, which is 13.6 per cent, and that of the Massachusetts General Hospital's 35 patients, which Dr. Richard Sweet tells me is 11.4 per cent.

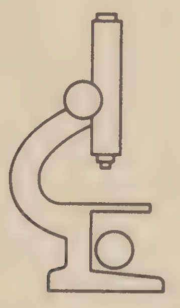
(*6*) The percentage of serious complications after lobectomy and especially after pneumonectomy is several times greater than that after thoracoplasty. Apparently the most serious and frequent are spread or reactivation of tuberculosis in remaining portions of the lung or lungs. Other potentially serious complications are empyema, bronchopleural fistula, tuberculous wound infection, tuberculous meningitis and persisting tuberculous infection of the bronchus at the site of its division.

(*7*) Pneumonectomy or lobectomy only rarely removes all the tuberculous lesions and a disappointingly large number of patients continue to have tubercle bacilli in their pulmonary secretions either from an ulcerated bronchial stump or from new, reactivated or old active parenchymal lesions.

(*8*) The late fatality rate and the percentage of apparent cures are not yet known in any large series of cases. In view of what I know of the late results in several small series of cases, I believe the late results in large series will be poor.

(*9*) The loss of function resulting from the removal of a whole lung, or even of only an upper lobe with varying degrees of fixation of the lower lobe from traumatic pleural effusion, is of clinical importance in a disease that is prone to late recurrence of activity.

(*10*) If, as I believe, the end results of pneumonectomy and lobectomy will prove to be far inferior to those of thoracoplasty in cases in which either type of operation might reasonably be used, I strongly recommend that neither pneumonectomy nor lobectomy be used in preference to thoracoplasty in any case unless the indications for resection are clear-cut and unless thoracoplasty is unlikely to succeed.



SURGICAL TREATMENT OF TENSION CAVITIES IN PULMONARY TUBERCULOSIS[1,2]

HERBERT C. MAIER

Collapse therapy has proved efficacious in closing a large percentage of tuberculous pulmonary cavities. It has been evident for several years, however, that some do not respond readily to collapse measures. Although the size of the cavity is of some importance, other characteristics are of perhaps greater significance. The intracavitary pressure plays an important rôle in determining the response to collapse therapy. Therefore tension cavities present a major problem in the treatment of pulmonary tuberculosis and account for a large number of the failures of pneumothorax and thoracoplasty. The pathological physiology of tension cavities will first be discussed briefly because rational therapy depends on an understanding of these fundamentals. The various types of surgical treatment for tension cavities will then be considered.

When caseation necrosis with excavation occurs in pulmonary tuberculosis, usually a more or less spherical defect in the lung occurs due to the elastic properties of the adjacent parenchyma. A small area of caseation may be followed within a week or two by a cavity of considerably greater size as demonstrated by serial roentgenograms. Thus, the size of the cavity does not indicate an equivalent area of pulmonary destruction. Although progressive peripheral caseation may be a factor in the enlargement of the tuberculous cavity, mechanical distension may also play an important rôle. The type of bronchial communication determines the facility with which air may enter or leave the cavity. The pressure within a pulmonary cavity may be either negative, atmospheric, or positive. A negative or an atmospheric pressure does not offer any obstacle to collapse therapy. A positive intracavitary pressure, however, may seriously interfere with closure by pneumothorax or thoracoplasty.

A positive pressure may develop due to a partial obstruction in the draining bronchus. The obstructive factor in the bronchial lumen may be either due to the involvement of the wall by a tuberculous process, the presence of tenacious secretion within the bronchial lumen or, perhaps, to spasm of the bronchial wall. Because the bronchus draining a tension cavity is often of small calibre, a slight alteration in the diameter of the bronchus may be of decided importance. As the bronchial lumen is normally larger during inspiration than during expiration, a check-valve mechanism may be produced in the draining bronchus. By this means, air can enter the tuberculous cavity during inspiration, but only a portion of the air can again escape during expiration. If there is a sudden increase in intrabronchial pressure, such as occurs in coughing, air may be forced into the cavity. This trapped air may then only escape intermittently. Although local factors in the draining bronchus are thought to be the cause of the

[1] From the Surgical Service of Triboro Hospital, Jamaica, New York.

[2] Presented before the Medical Section at the 40th annual meeting of the National Tuberculosis Association, Chicago, Illinois, May 11, 1944.

development of tension cavities, the frequent occurrence of multiple tension cavities in the same patient raises the question of some systemic influence. Whether this is due to some diffuse alteration in the bronchial wall or whether an element of spasm plays a rôle can only be conjectured at this time.

A large tension cavity may represent a defect in the lung which has been produced by a relatively small area of caseation necrosis with liquefaction. This is then inflated to large size by the trapping of air within the cavity because of the check-valve mechanism in the draining bronchus. Such cavities may therefore vary greatly in size over short periods of time. In some instances there is little change over a period of months or even years; but should an alteration in the check-valve mechanism of the draining bronchus occur, the size of the cavity may change rapidly. If the draining bronchus becomes completely obstructed, the air trapped within the pulmonary cavity will be absorbed and a negative rather than a positive pressure within the cavity will result. Marked shrinkage or complete obliteration of the cavity may then follow. If the check-valve mechanism of the draining bronchus is replaced by a free bronchial communication on inspiration and expiration, the positive pressure in the cavity will disappear. Under these circumstances, there will tend to be a reduction in its size, although usually not closure.

In many cases of cavitation in pulmonary tuberculosis there may be a difference of opinion concerning the recognition of a tension cavity on the basis of the roentgenogram alone. In other instances the behavior of the cavity over a period of time, as indicated by serial roentgenography, may conclusively demonstrate the pressure characteristics of the cavity. Although occasional observations of pressure readings of tuberculous cavities have been reported in the literature for a number of years, it is only recently that detailed observations of pressure readings on intrapulmonary cavities have been made. Eloesser (2), and Brunn and his coworkers (1) have published interesting observations on intracavitary readings in pulmonary tuberculosis. Riggins and Gearhart (3) made studies of intracavitary pressures. In some cases the same cavity was studied on a number of occasions over a considerable period of time. They have shown that, whereas a positive intracavitary pressure may exist at one time, the pressure may be less positive, atmospheric or even negative at another time. These alterations may occur spontaneously or be associated with collapse therapy or intracavitary drainage. As previously mentioned, the changes in the intracavitary pressure are secondary to alterations in the bronchial communication.

Until recently, needling of tuberculous cavities was thought to carry considerable hazard. By a careful technique, however, it has been shown that this procedure can be carried out with relatively little risk. Vineberg and Kunstler (4) recently reported 150 instances of needling of cavities in 62 cases. No ill effects and no complications occurred; that is, all needlings were accomplished without development of air embolism, empyema or gross hemorrhage. It should be emphasized that these good results can only be obtained if meticulous technique in needling is employed. Moreover, the introduction of any material

into the tuberculous cavity such as lipiodol would seem to increase the hazard. The injected material, mixed with secretion, may escape through the bronchial communication and thus occasionally cause a bronchogenic spread of the tuberculosis.

The behavior of tension cavities is unpredictable. Although it is known that this type of cavity is an important cause of failure of collapse therapy in pulmonary tuberculosis, such a cavity may nevertheless, at times, respond well to collapse treatment. Riggins and Gearhart (3) have determined the intracavitary pressure in cases which were later subjected to various types of therapy. In a few instances even a huge tension cavity disappeared spontaneously without any therapy other than bed-rest. A similar sequence of events has occurred occasionally in previous years when diaphragmatic paralysis was employed even for large cavities. The disappearance of a large cavity following either bed-rest alone or after diaphragmatic paralysis cannot be considered as necessarily due to the type of therapy given. It seems more probable that a chance alteration in the bronchial communication of the cavity, which may or may not have been influenced by the general or local rest treatment, caused the dramatic result. Moreover, similar spontaneous cavity closure may occur without any treatment whatsoever.

Tension cavities respond better to thoracoplasty than to pneumothorax therapy. This difference in result is not due to a difference in the degree of collapse obtained by the two methods of treatment. A balloon cavity remaining in a lung almost completely collapsed by pneumothorax may later be closed by a thoracoplasty. This result may be obtained although the thoracoplastic collapse is less complete than that previously accomplished by pneumothorax. It is therefore evident that the degree of collapse is not necessarily the deciding feature. The immobility of the thoracic cage with practical elimination of lung motion which follows extensive thoracoplasty may be an important factor. Because of the lack of mobility of the lung and bronchial tree under thoracoplasty, there may be a greater tendency to more complete blockage of the bronchus. In a number of cases of tension cavities subjected to thoracoplasty, I have noted a rising fluid level within the cavity. This indicated further impairment of bronchial drainage. In some such instances the site of the cavity was later replaced by a uniform opacity on the roentgenogram. Undoubtedly in these cases the cavity became filled with inspissated material rather than closed by apposition of its walls. The sputum might become negative, associated with the disappearance of the highlight on the roentgenogram. This conversion of sputum again was merely due to complete obstruction to cavitary drainage.

When a thoracoplasty is performed over a tension cavity it is not unusual to note persistence of the cavity immediately following conclusion of the series of operations. What at first seems to be a failure of thoracoplasty may some months later appear to be a satisfactory therapeutic result because of cavity closure under thoracoplasty. Although in the past closure of tension cavities under the thoracoplastic collapse has been attributed to contraction of fibrous

tissue within the lung, this seems to be an unsatisfactory explanation. Again the obstruction of the draining bronchus would seem to be the deciding feature.

Tension cavities subjected to pneumothorax therapy frequently enlarge as the lung is collapsed. Conversely, a large tension cavity in a well collapsed lung may become much smaller or disappear when the pneumothorax is abandoned. It has long been recognized that if pneumothorax therapy failed to accomplish cavity closure the percentage of cavity closure by later thoracoplasty was greater if the lung was first reëxpanded before thoracoplasty was performed. If a markedly negative intrapleural pressure exists during pneumothorax therapy, it is readily understandable that the pressure gradient between the inside of the cavity and the pleural space would favor enlargement of a thin-walled cavity. Occasionally a positive pressure pneumothorax will temporarily compress the tension cavity. Vineberg and Kunstler (4) advocated routine needling of tuberculous cavities over 2.5 cm. in size. If a tension cavity was proved to exist, decompression by intracavitary suction drainage was considered indicated. A preliminary stage of thoracoplasty to remove the ribs in the area in which the catheter was to be introduced was first carried out. Then the catheter was introduced and intracavitary suction maintained. Later the thoracoplastic procedure was completed.

Although it is known that tension cavities are responsible for a considerable percentage of the therapeutic failures by thoracoplasty, the presence of a tension cavity does not necessarily mean that thoracoplasty will fail to close it. I am unaware of any series of cases of tension cavities treated either by pneumothorax or thoracoplasty in which both early and late results have been evaluated. Not infrequently an early, apparently excellent therapeutic result may prove to be a failure one or more years later. We have seen cavities which apparently closed on reëxpansion of an unsuccessful pneumothorax, reopen at a later date. In such a case the late failure might be ascribed to the fact that the lung was reexpanded. Nevertheless, a similar occurrence has been noted under thoracoplasty. The cavity which at one time was closed may later reopen to large size in spite of a good thoracoplastic collapse. Therefore, in addition to the early results of collapse therapy for tension cavities being unsatisfactory, it must also be realized that the late results may be even less satisfactory.

Theoretically, it might seem most logical to treat tension cavities by decompression and later follow with thoracoplastic collapse. Several objections to this program must be mentioned. Even prolonged intracavitary suction drainage does not necessarily alter the condition of the draining bronchus of the cavity. Therefore, the possibility remains that at any time the cavity may reopen and again assume pressure characteristics. The Monaldi procedure may result in apparent closure of the cavity with conversion of the sputum, but even after subsequent thoracoplasty, performed to maintain closure, the cavity may reopen to large size. As far as I know, the literature does not contain any large series of cases in which intracavitary suction drainage was followed by thoracoplasty and the final results evaluated. Unless the reports limit the discussion of final results to cases in which all wounds and fistulae are closed, the program of treat-

ment cannot be completely evaluated, even as far as early results are concerned. Moreover, intracavitary suction drainage has been in use too short a time to permit evaluation of its late results in the early apparently successful cases.

Another objection which may be advanced against the routine application of intracavitary suction drainage prior to thoracoplasty, whenever an intracavitary reading has demonstrated the presence of a tension cavity, is the considerable percentage of cases which are thus needlessly subjected to a long period of therapy prior to thoracoplasty. In a considerable percentage of cases in which a Monaldi drainage has been successful when followed by thoracoplasty, the question arises whether the thoracoplasty alone might not have yielded a similar result.

When a thoracoplasty has failed to close a tension cavity, a secondary drainage of the cavity may be considered. The collapsed state of the pericavitary portion of the lung, however, may influence the response to suction drainage. If the adjacent pulmonary tissue has been collapsed by thoracoplasty for a considerable period of time, the possibility of reinflation and filling in the site of cavitation is reduced. In my experience, considerable difficulty has been encountered in obtaining cavity closure and complete wound healing following secondary cavernostomy after thoracoplasty.

If the pulmonary tuberculosis is limited chiefly to one lobe of the lung in which the tension cavity is located, the feasibility of pulmonary lobectomy must be considered. Although such a therapeutic program could hardly have been deemed advisable a few years ago, the situation is now somewhat different. The technique of lobectomy employed until the past few years involved leaving a stump of pulmonary tissue at the hilum. This residual pulmonary tissue usually contained tuberculous foci which were traumatized in the course of the operative procedure. Moreover, at that time the incidence of bronchial fistula after lobectomy performed for nontuberculous lesions was high. Therefore, lobectomy and pneumonectomy in the presence of active tuberculosis was regarded as an extremely hazardous procedure. Whereas these same potential dangers still exist to-day, refinements in surgical technique now permit in many cases a clean and meticulous surgical dissection of the individual pulmonary lobes. Therefore, at the present time, it is possible under ideal circumstances to perform pulmonary resection for active pulmonary tuberculosis with a reasonable fatality rate and only moderate danger of postoperative bronchial fistula and empyema. Recent advances in anesthesiology have permitted this meticulous and painstaking type of operative intervention and have lessened the dangers of tuberculous spread during operation. Therefore, at this time, it is appropriate to consider the treatment of tension cavities by pulmonary resection.

I have performed 16 lobectomies by hilar dissection for pulmonary tuberculosis in patients with positive sputum. In half of the cases a tension cavity was the indication for pulmonary resection. Ten patients had an entirely uncomplicated postoperative course. In 3 patients a previously existing lesion in the contralateral lung showed a transient perifocal flare-up. One of these cleared within a week. In the 2 patients in whom the contralateral reactivation was

more prolonged, both had sufficient disease in the contralateral lung to contraindicate thoracoplasty. Only 2 empyemata occurred, one of which was tuberculous while the other was pyogenic. A transient bronchial fistula was present in only the 2 empyema cases. There was one fatality in the entire series; death occurred a month following operation due to a contralateral tuberculous spread. At this time, all except 2 of the patients have a negative sputum, but in one additional case the operation is too recent to evaluate the sputum findings. To date 2 late complications have arisen. One patient, who left the hospital against advice five weeks after lobectomy and resumed a very active life, returned a few months later with reactivation in the lower lobe following a lobectomy of the left upper lobe. Another patient had a contralateral pleurisy several months following lobectomy, but this has since cleared.

I have performed 2 pneumonectomies for tension cavities. In one case even a revision thoracoplasty had failed to close the cavity. The other patient had failed to obtain cavity closure by pneumothorax. Both patients had an uneventful postoperative course.

The recent results of pulmonary resection in the treatment of tension cavity have been encouraging. Considerably more experience and a more prolonged follow-up will be necessary before the procedure can be properly evaluated. Moreover, pulmonary resection for tuberculosis requires a surgical set-up which is available in only a limited number of hospitals at this time.

SUMMARY

The pathological physiology of tension cavities has been briefly discussed. The advantages and disadvantages of various surgical procedures in the management of pressure cavities have been considered. The results of pulmonary resection are presented.

REFERENCES

(1) Brunn, H., Shipman, S., Goldman, A., and Ackerman, L.: Tuberculous cavitation and transpleural decompression, J. Thoracic Surg., 1941, *10*, 485.

(2) Eloesser, L.: The choice of procedure in the treatment of tuberculous cavities, J. Thoracic Surg., 1941, *10*, 501.

(3) Riggins, H., and Gearhart, R. P.: Studies of the Pathogenesis, Dynamics, and Closure of Tension Cavities, presented at the meeting of the American Association for Thoracic Surgery, Chicago, May 6, 1944.

(4) Vineberg, A. M., and Kunstler, W. E.: The determination and treatment of pressure cavities in pulmonary tuberculosis, Surg., Gynec. & Obst., 1944, *78*, 245.

TOTAL PNEUMONECTOMY FOR PULMONARY TUBERCULOSIS*

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WHAT are the indications for lobectomy or pneumonectomy in pulmonary tuberculosis? Eloesser, Alexander, Churchill, and others agree that hemorrhage and suppuration complicating tuberculosis of the lungs, stenosis of the bronchus, persistent cavities after thoracoplasty, rare unilobular basal cavity, atelectasis, absence of ulcerative bronchial disease, failure of the collapse therapy, and last but not least a good contralateral lung, all point to the advisability of lobectomy and pneumonectomy. After the communication by Jones and Dolley in 1939, read before the American Association for Thoracic Surgery, the profession was stirred by the revelation that several patients had been operated upon for tuberculosis of the lungs, while at the same time others were found to be tuberculous following a pneumonectomy performed under a mistaken diagnosis. It is well known that carcinoma and tuberculosis may be present in the same patient. In one of our cases, tubercle bacilli were found in the sputum for the first time after pneumonectomy. It has become evident that many cases wholly unsuitable for lobectomy and pneumonectomy were selected for operation in the past. Obviously an ulcerated bronchus must first be treated to prepare the patient for operation. After treatment a constriction of the bronchus may result, damming up secretions in the lung. The stricture of the bronchus may cause enlargement of existing cavities, filling them with pus which cannot be expectorated. The cavities are naturally filled most of the time, and never completely emptied, thus giving rise to toxic symptoms of chills, fever, malaise, and weakness. There are some cases in which normal temperature has been present for a long time. These can well be compared to a localized area of pus in a closed cavity. With the constricted bronchus, little or no expectoration is recovered. The reflex of coughing is present but it is unproductive. Cases chosen for lobectomy or pneumonectomy should be limited to chronic ulcerative tuberculosis of the bronchus without involvement of the contralateral lung. Emphysema of the contralateral lung is a natural sequel following atelectasis of the opposite side.

REVIEW OF LITERATURE

This review of the literature comprises cases in which the patients were operated upon for pulmonary tuberculosis.

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In 1938, Overholt reported a pneumonectomy for tuberculosis. He states that if the tuberculous process is quiet at the time of resection, healing should be prompt. Samson stated that pneumonectomy should be considered in a high-grade bronchial obstruction with complete atelectasis and fibrosis of the lung. Bronchial lesions should be quiet, as active advancing ulcerative disease is a contraindication. Overholt (1939), in a very comprehensive communication on the subject of pneumonectomy, reports several surgeons who have performed this operation for tuberculosis. The reports are rather discouraging, but one must take heart when one considers that these were the pioneer operations. The results are better now. Archibald, Lindskog, Arce, Rienhoff (two cases), and Crafoord (three cases), 1935-1938, performed pneumonectomy for tuberculosis with bronchiectasis in some cases. The patients in only two cases, those of Crafoord's, were well at the end of three years and ten months, respectively. All others died from two hours to three months after operation.

Jones and Dolley (1939) feel that preliminary thoracoplasty is important in removal of the lung for tuberculosis. When the sputum remains positive after thoracoplasty they feel that resection of the lung should be performed if the hazard is not too great. Contralateral spread is the greatest danger. They now admonish greater caution in the selection of cases. In 1939, they report pneumonectomies on four of their patients. Two died from contralateral spread. The other two lived but were not cured. Jones and Dolley refer to cases in which the patients were operated upon by Block (1881, died) (bilateral upper lobe lobectomy) and Ruggi (1885, two patients died). Tuffier, in 1891, removed the apex of the lung and presented the patient as cured in 1895. In 1935, Eloesser and O'Brien each did a one-stage lobectomy; spread of tuberculosis caused death in both patients. Lindskog (1937) removed a lung for bronchiectasis which was later found to contain evidence of tuberculosis. Heuer collected nine cases in which lobectomy had been performed for tuberculosis from 1880 to 1920. Freedlander, after 1920, removed the right upper lobe for tuberculosis.

Graham, in 1913, removed a large portion of the right lung for chronic suppuration. The pathologic examination revealed also the presence of tuberculosis; the patient was alive eight years after. James performed a lobectomy for a cavity which remained open; the result was unsatisfactory. Corryllos performed a lobectomy in two cases with unsatisfactory results. Urquhart operated for a stricture of bronchus present five months; the patient died. Harrington performed a lobectomy for bronchiectasis with tuberculosis of the upper lobe. Dolley and Jones (1935) performed the following operations in sequence on the same patient: right pneumothorax, phrenemphraxis, thoracoplasty after stenosis of right stem bronchus, and tourniquet pneumonectomy, followed by good recovery. Dieffenbach performed a pneumonectomy in

1939; the patient remained well without contralateral involvement. Tuttle performed lobectomy in a girl 15 years old; she died from non-tuberculous pneumonia in the contralateral lung. Freedlander performed lobectomy in 1938 in a young girl; results were satisfactory. He did the operation of lobectomy in three other patients, one for empyema and bronchial fistula; another died from spread of the disease after operation, and the third recovered. An aberrant accessory lobe was the seat of cavitating tuberculosis. Leahy performed a lobectomy, with recovery, on a patient who had chronic pulmonary tuberculosis with bronchiectasis but without cavitation. Adams did a lobectomy for tuberculosis of the lower lobe in a woman 19 years old; convalescence was good except for a small empyema. Bigger reports a women, 29 years old, who had had tuberculosis for nine years. She was well for four years after an extensive thoracoplasty; ulceration of the right stem bronchus followed and a pneumonectomy was performed. She is working at the time of this communication, as a technician.

Churchill (1940) states that advance in treating the tuberculous lung has been enhanced more by operations performed through mistaken diagnosis than by deliberately planned operations. In addition he says bronchial stenosis is the strongest indication for operation. Any other treatment is futile Blocked cavities and the failure of collapse therapy are also indications for lobectomy or pneumonectomy. Five lobectomies were done for tuberculosis, with one death.

In the case reported by A. Behrend (1941) the frequently reported coexistence of carcinoma and tuberculosis was noted. In his case, tubercle bacilli were found in the sputum for the first time after pneumonectomy.

According to John Alexander (1941), too few patients fulfill the conditions that permit a lobectomy or pneumonectomy. These are open cavities after thoracoplasty, absence of ulcerative bronchial disease, and a good contralateral lung. He performed one successful pneumonectomy in about 1937. The two patients who had lobectomies done are well, one and two years after operation. Graham believes that no patient has unilateral tuberculosis. He has performed four upper lobectomies with good recovery, and one lower lobectomy which was fatal. Eloesser advocates lobectomy for blocked cavities. He performed a pneumonectomy on a patient not suspected of having tuberculosis, who died five months later from a secondary tuberculous empyema. One successful lobectomy for tuberculoma of the lower lobe was performed. Butler carried out a pneumonectomy but he stated it was too early to report on the outcome of the case. Raine performed pneumonectomies on three patients; all died. Lewis operated on two patients for primary tuberculous pneumonia. One case proved not to be primary tuberculous pneumonia and the patient died. The second patient was operated upon with tourniquet ligation of the lobe of the lung, and this patient re-

covered. Buckingham performed two pneumonectomies; one patient died of ileus, one was able to be up and about with a fistula. J. A. Moore reports one pneumonectomy in which the patient died four months after operation of acute anemia. Lobectomy was successful following a two-stage thoracoplasty; the patient had tuberculosis for seven years. Moore believes that a preliminary thoracoplasty would minimize the danger of empyema. Three lobectomy patients were cured.

Chamberlain and Gordon admit that external drainage of a cavity due to bronchial stenosis is occasionally necessary. Pneumothorax is not advocated. Lobectomy and pneumonectomy may be performed in some cases followed by thoracoplasty. Berry believes pneumonectomy is indicated in certain selected cases with a healed stenosed bronchus. He performed pneumonectomies on two patients with advanced chronic pulmonary tuberculosis.

TABLE I

NUMBER OF PATIENTS TO DATE OPERATED UPON FOR TUBERCULOSIS OF THE LUNGS*
(1881-1942)

LOBECTOMY			
	TOTAL CASES	LIVING	DEAD
Churchill	5	4	1
Alexander	3	3	0
Graham	5	4	1
J. A. Moore	1	1	
Freedlander	4	3	1
Leahy	1	1	
Adams	1	1	
Block	1		1
Ruggi	2		2
Tuffier	1	1	
Eloesser	1		1
O'Brien	1		1
J. Shipman	1	unsatisfactory	
James	1	unsatisfactory	
Corryllos	2		2
Urquhart	1		1
Harrington (result not reported)	1		
†Skinner and Macpherson	1	1	
Lewis	1	1	
Total	34	20	11

PNEUMONECTOMY			
	TOTAL CASES	LIVING	DEAD
Dolley and Jones	4	2	2
Alexander	2	1	1
Eloesser	1		1
Butler (too early to report)	1		
Raine	3		3
Buckingham	2	1	1
J. A. Moore (lived 4 mo.)	1		1
Dieffenbach (well after 3 yr.)	1	1	
Tuttle	1		1
Bigger	1	1	
Overholt	1	1	
Archibald	1		1
Lindskog	1		1
Arce	1		1
Rienhoff	2		2
Crafoord	3	2	1
Berry	2		2
Dolley and Jones	1	1	
M. Behrend	1	1	
Total	30	11	18

*Authors mentioned in this table are referred to in the list of references.
†Personal communication.

Tuttle, O'Brien, Day, and Phillips (1942) report ninety-two cases of constrictive or ulcerative type of bronchus. In these cases pneumothorax or thoracoplasty was used. They do not advocate pneumonectomy on account of the discouraging reports following this operation. Phrenic operations should not be performed on these patients. Alexander, Sommer, and Eller (1942) stress the indications and contraindications to thoracoplasty and pneumonectomy in the treatment of pulmonary tuberculosis with bronchial stricture, atelectasis, and fibrosis.

They advocate thoracoplasty provided there is no contraindication. They report the results of thirty-eight patients operated upon in a five-year period. They admit the indications for pneumonectomy and lobectomy are rare. One patient in whom a pneumonectomy had been performed was living five years after operation. Another patient died thirteen days after operation from rupture of an ulcerative aorta.

SYMPTOMS

The symptoms that result from these changes cause long years of invalidism with attending inability to perform the usual duties of everyday life. Tubercle bacilli may be present intermittently for the duration of life. Again, sputum may become negative with the passing of years and remain negative up to and including the time of the contemplated operation on the lobe or the lung. These are the most favorable patients for operation, especially those who have no semblance of contralateral involvement. It is my impression that the negative sputum is due to stenosis of the bronchus, poor drainage, and compression of the cavities due to atelectasis.

SELECTION OF CASE

On our service, the first suitable patient for pneumonectomy suffering from tuberculosis of the lungs presented herself in November, 1941. Occasionally after a patient has had a thorough selective stage thoracoplasty the sputum remains positive, a most discouraging feature. This may be due to a cavity that has not been decompressed, or the cavity may be in direct communication with a bronchus, or the bronchus may be ulcerated and stenotic. It has been stated that a thoracoplasty should be performed before the operation of lobectomy and pneumonectomy is performed. Thoracoplasty was not done in our patient. This technique need not be followed when an obstruction has existed in the bronchus for a long time and a progressive atelectasis has resulted causing deficient expansion with a natural diminution in the size of the hemithorax. This is an added advantage to the ultimate recovery of the patient because of the diminished size of the thoracic cage. Such a condition was encountered in the case about to be reported.

OPERATIONS

The two operations of choice for open cavities that cannot be drained as a result of stenosed bronchi causing retention of secretions are lobectomy and pneumonectomy; the ideal procedure is pneumonectomy, provided of course the contralateral lung is entirely free of tuberculosis. Graham believes there is no unilateral tuberculosis. In conjunction with A. Behrend we have performed nine pneumonectomies with the anterior incision according to the technique of Rienhoff. I prefer now the posterolateral incision as advocated by Overholt. More room is obtained for the separation of adhesions if present and for the individual ligation of structures at the hilum.

The following case fulfilled all the conditions required for the performance of a pneumonectomy.

L. M., a nurse, aged 45 years, had been admitted Sept. 8, 1937, and discharged improved on June 19, 1938 (Fig. 1). She was readmitted Nov. 6, 1941.

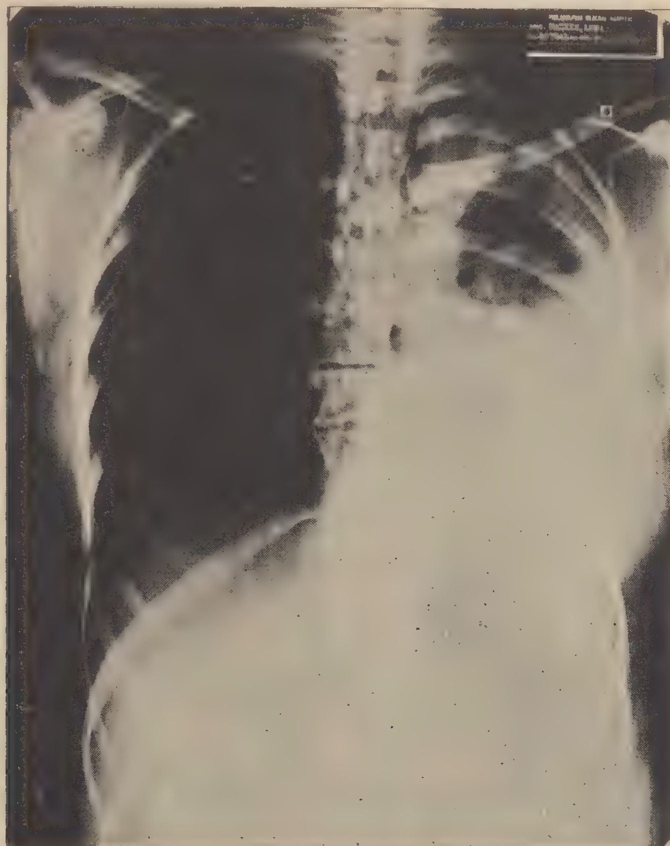


Fig. 1.—Atelectasis of lung. A small cavity can be seen in the left upper lobe; pneumothorax gave only a fair collapse.

Diagnosis of pulmonary tuberculosis was established by x-ray March, 1937. At the time of admission she had atelectasis of the left lower lobe due to stenosis of the bronchus. A small cavity in the left upper lobe was present with repeated positive sputum. Pneumothorax gave a fair collapse with closure of cavities, and the sputum became negative. Repeated bronchoscopic examinations revealed stenosis of the bronchus. Dilatation of the bronchus was never entirely successful in emptying of cavities. Thoracoplasty was decided against. The patient was discharged June 19, 1938, with a diagnosis of tuberculosis of the left lung; advanced stenosis of left bronchus. She was treated at home where sputum was negative for acid-fast bacillus for about three years. Repeated bronchoscopic dilatations were necessary, however. These treatments were given every six weeks.

In August, 1941, bronchoscopic treatment was necessary every two weeks and was continued up to the time of admission in November, 1941. At the patient's insistence she was admitted for possible pneumonectomy

or lobectomy. Weight had remained in the vicinity of 116 pounds. She had had no night sweats, afternoon fever, or hemoptysis. During the last two months before operation she became dyspneic at rest and on mild exertion, with frequent nonproductive paroxysms of coughing. She required several pillows on which to sleep. Her appetite was good; there was no indigestion and no jaundice. Temperature at this time was normal, pulse 100, and respiration 25.

Physical Examination.—Chest: Breasts small, no masses or discharge. Thoracic cage showed flattening of left anterior chest below the clavicle to seventh and eighth ribs. The left chest lagged on inspiration. The right lung was emphysematous, percussion resonant to hyperresonant. No râles or adventitious sounds were heard. The heart was drawn to the left. Apex beat was in the fourth interspace, precordium was quiet, and no murmurs were heard. The veins of the neck were not distended.

Examination of the heart on Nov. 10, 1941, by electrocardiogram (P. M. McMillan) revealed a right axis deviation and a simple tachycardia. These did not justify any definite conclusions. The heart was displaced to the left. This was verified by the fluoroscope, which showed the heart to be entirely in the left chest. We could find nothing else, and we believe this to be a normal heart except for its displacement.

Vital capacity by Haslem-Smyth Spirometer gave: Trial 1, 135 cubic inches; trial 2, 140 cubic inches; and trial 3, 135 cubic inches. Normal average is 190 cubic inches, therefore the patient's vital capacity was 75 per cent normal. Blood examination revealed R.B.C., 4,500,000; W.B.C., 10,600; polymorphonuclears, 84; and urine negative.

On Nov. 7, 1941, x-ray report by H. Ostrum showed (Fig. 2) practically no change when compared with previous examination, July 8, 1941. The right lung was normal except for some compensatory emphysema. There was atelectasis of the left lower lobe and fibroid tuberculosis of the left upper lobe.

At a therapy conference Nov. 19, 1941, C. A. Heiken presented the case to the staff meeting for a total pneumonectomy.

L. Clerf reported that a large quantity of thick, mucopus was found coming from the left bronchus. The lumen of the stenosed bronchus was not more than 3 or 4 mm. in diameter. There was present moderate inflammatory reaction. The stenosis was about 2 cm. beyond the carina. Clerf also recommended pneumonectomy.

By Nov. 25, 1941, the patient was in good condition preoperatively. Pneumothorax was performed, but rather ineffectively since only 150 c.c. were injected.

Operative Note, Nov. 28, 1941: Operation was performed under cyclopropane, intratracheal anesthesia. During the operation 400 c.c. of blood and 800 c.c. of saline solution were given. At the beginning of operation, blood pressure was 130/75.

Description of operation: A posterolateral incision was used. A portion of the seventh rib was excised. About one inch of the sixth and eighth ribs at the angles were excised. Rienhoff's retractors gave the desired space for the completion of the operation. The lung was atelectatic, adherent at the apex, laterally, and to the diaphragm. The adhesions were separated rather easily. Individual separation of the structures at the hilum was begun; the vessels and bronchus were ligated in

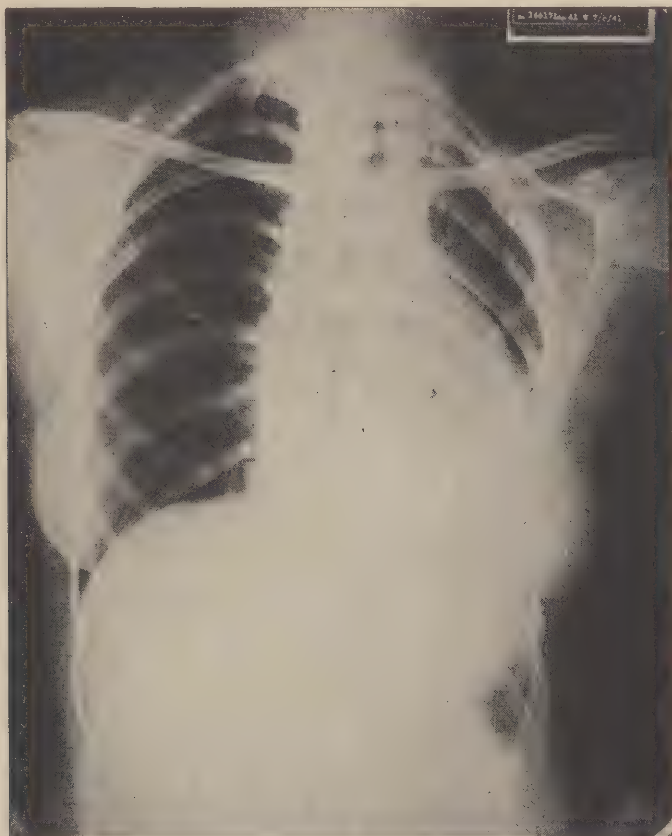


Fig. 2.—X-ray July 8, 1941 showed atelectasis of the lower left lobe and fibroid tuberculosis of the left upper lobe; right lung was normal.

their proper order. All ligated structures were covered with pleura after 5 Gm. of sulfanilamide were dusted over these structures. No drainage was employed. The patient was returned to her room in moderate shock and at 7 P.M. she was in shock. Plasma, 350 c.c. was given. At 11 P.M. blood pressure was 86/60 and she was in better condition. Fluids were discontinued.

On Nov. 29, 1941 the patient was in good condition. Temperature was 98, pulse 120, respiration 22. The right lung was clear; blood pressure 114/60. A blood transfusion of 450 c.c. of blood and 500 c.c. of 5 per cent glucose in saline was given.

On Dec. 13, 1941, there was a postoperative effusion which started shortly after operation but was never aspirated because there was no sign of infection.

X-ray (Fig. 3) by H. Ostrum, Dec. 22, 1941, showed the right lung clear. There was hydropneumothorax on the left side with fluid level just beneath the clavicle; heart was normally situated.

Pathologic Report.—Gross description by Harold M. Dixon on Nov. 29, 1941, revealed the specimen as an unfixed left lung removed in toto, measuring 15 by 8 by 6 cm. The pleura was rough, thick, and dull red. The consistency of both lobes was fleshy, and there were numerous ill-defined firm areas 2 to 3 cm. in diameter in each lobe. On cross section, these consisted of thickened dilated bronchi with gray purulent contents and surrounding fibrosis. There were two thin-walled cavities in the upper lobe posteriorly, measuring 1 to 2 cm. in diameter, filled

Fig. 3.—Dec. 22, 1941, after operation. There was hydropneumothorax on the left side with fluid level beneath the clavicle. The heart was normally situated and the right lung clear.

with thick caseous gray material and lacking communication with bronchi. Numerous other thin-walled cavities less than 1 cm. in diameter were present, but communicated directly with dilated bronchi. The bronchial dilatation, thickening and surrounding fibrosis, affected all the bronchi, extending to the periphery of the lung. There was no grossly recognizable normal lung tissue. Apparently, the main stem bronchus had been severed below the point of stenosis. Impression: Bronchiectasis with atelectasis and fibroid tuberculosis.

Microscopy (Fig. 4).—The usual architecture of the lung was considerably distorted due to fibrosis, dilatation of bronchi, and chronic inflammation of the peribronchial areas. Along some edges and in the substance of the lung parenchyma, large areas of caseous necrosis were noted, with epithelioid cells. The dilated bronchi contained leucocytes but were lined with columnar epithelium.

Pathologic Diagnosis: Fibrocaseous tuberculosis with bronchiectasis.

Fig. 4.—Fibrosis of lung, dilatation of bronchi chronic inflammation of peribronchial areas. Large areas of caseous necrosis. Several Langhans type giant cells.

Comment.—This was an ideal case for the operation of total pneumonectomy because it met many of the postulates necessary for such a procedure. The cooperation of the patient, her desire to be operated upon rather than live the life of an invalid, contributed much to the ultimate successful result. The convalescence was absolutely uneventful. Next morning the patient appeared as though no operation of such magnitude had been performed the previous day. The temperature was practically normal, the pulse was a little rapid, the respirations were not increased. The patient left the hospital eight weeks after operation and remained well thereafter. There is still some effusion present on the left side. No drainage was employed. I much prefer not to drain after total pneumonectomy. There are some cases, however, where this aid must be used. The fluid following the operation was never aspirated. The heart remained in normal position and there was no shift of the mediastinum. Dyspnea was absent.

April, 1943, eighteen months following the operation, the patient was in good health.

Dolley and Jones advocate the importance of thoracoplasty previous to removal of a tuberculous lung. They were very enthusiastic in their early reports concerning lobe and lung removal, but in their later communications they admonish greater caution in the selection of cases. Thoracoplasty was not considered necessary in the case reported above. There was a natural narrowing of the left thorax as a result of a chronic atelectasis.

CONCLUSIONS

1. A case of pulmonary tuberculosis in which a total pneumonectomy was performed is presented. Intratracheal cyclopropane anesthesia was used.

2. April, 1943, eighteen months since the operation, the patient is in good health.

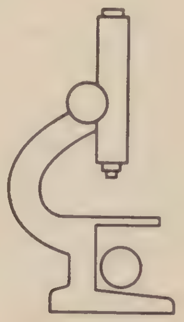
3. Consideration is given to the operations of lobectomy and pneumonectomy.

4. Thoracoplasty as a preliminary procedure is not considered necessary.

5. The literature is reviewed.

REFERENCES

1. Overholt, Richard: Surg., Gynec. & Obst. **66**: 328-336, 1938.
2. Idem: J. Thoracic Surg. **9**: 17-61, 1939.
3. Dolley, Frank S., and Jones, John C.: J. Thoracic Surg. **8**: 351-370, 1939.
4. Dolley, Frank S., and Jones, John C.: J. Thoracic Surg. **10**: 102-121, 1940-41.
5. Graham, Evarts A.: Surgery **8**: 239-246, 1940.
6. Churchill, Edward D.: Surgery **8**: 961-991, 1940.
7. Behrend, Albert: Pennsylvania M. J. **44**: 1156-1158, 1941.
8. Berry, Frank B.: Ann. Surg. **114**: 32-45, 1941.
9. Behrend, Moses, and Behrend, Albert: Arch. Surg. **38**: 698-713, 1939.
10. Alexander, John: Editorial, Am. Rev. Tuberc. **44**: 765-767, 1941.
11. Chamberlain, J. M., and Gordon, Joseph: J. Thoracic Surg. **11**: 292-298, 1942.
12. Tuttle, W. M., O'Brien, E. J., Day, J. C., and Phillips, F. J.: J. Thoracic Surg. **11**: 299-307, 1942.
13. Alexander, John, Sommer, George H. J., and Ehler, Adrian A.: J. Thoracic Surg. **11**: 308-325, 1942.
14. Heuer, George J.: J. Thoracic Surg. **3**: 560, 1934.
15. Samson, Paul C.: Discussion, J. Thoracic Surg. **10**: 119-120, 1940.



LOBECTOMY FOR PULMONARY TUBERCULOSIS

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and

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"Resection of lung tissue is very hazardous in the presence of a positive sputum. If possible collapse therapy is preferred." This is the conclusion drawn from a compilation of the recorded cases of pulmonary resection for tuberculosis by recent authors.[3] In as rapidly developing a field as thoracic surgery, impressions drawn from past experience are notoriously misleading. This is particularly true if a reportorial account of experience is taken at its face value, without critical analysis.

The assembled cases of tuberculosis in which pulmonary resection has been carried out form an exceedingly heterogeneous group. Of 80 cases recorded as having been subjected to pneumonectomy or lobectomy, 30 came to operation with an erroneous diagnosis. This can only mean that the preoperative estimate of the situation and, consequently, the time of operation and the technics employed were not in terms of the pathology of tuberculosis. These operations were not performed "for" tuberculosis—the true nature of the disease was discovered too late for the observance of important elementary principles.

Twelve other cases were operated upon after collapse therapy had failed—always an added technical burden. Other cases were resected because of bronchiectasis, intractable hemorrhage, or in the presence of the fever and toxicity of bronchial strictures.

In the lobectomy group no reference to the surgical technics employed is made. Kent and Blades[2] conclude from their anatomic dissections that the application of individual ligation technic to the right upper lobe is possible, but appear to know of only one instance in which lobectomy has been thus performed. These authors state that as far as the left upper lobe is concerned, "except under unusually favorable circumstances, the individual ligation technic for resection will be hazardous or impossible."

Resections of upper lobes, both right and left, by individual ligation

technics have been routinely performed in this hospital since 1936, and total 21 in number.

While it seems unlikely that the opinions of Kent and Blades reflect a general belief, they at least suggest that a considerable number of the lobectomies for tuberculosis collected by Thornton and Adams[3] may have been carried out by the tourniquet technic. This is a procedure eminently successful in bronchiectasis but if applied to a tuberculous lesion would seem predestined to invite empyema, bronchial fistula, or both.

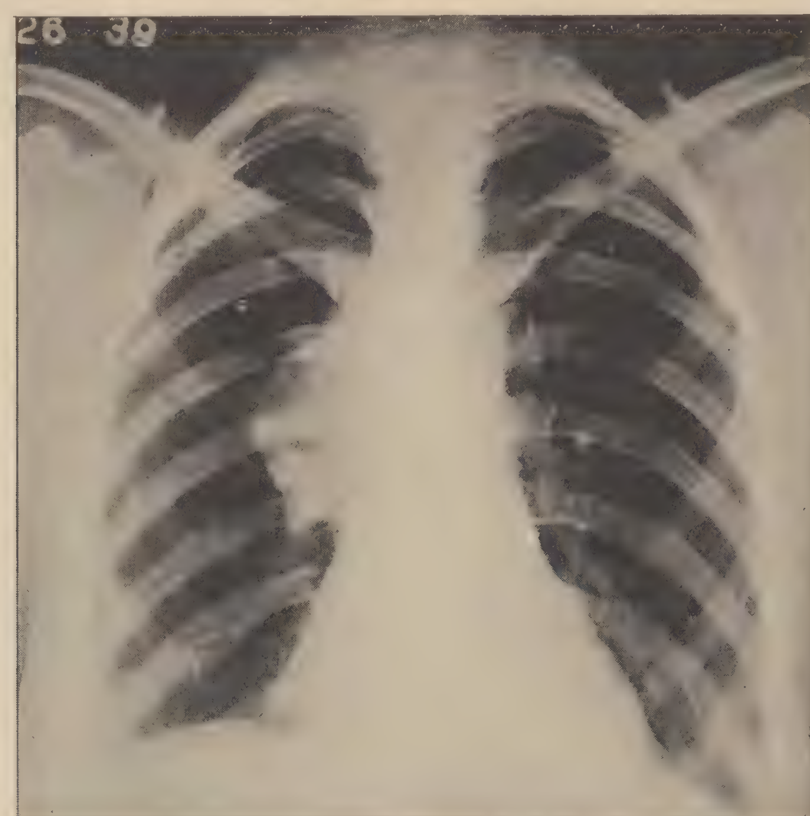


FIG. 1a.—Preoperative, May, 1939. Oval shadow of increased density in the apex of the right lower lobe. An irregular cavity present in the mass.

Not content to accept a conclusion based on the disasters and prejudices of the past, it seems desirable to present new evidence regarding what may be accomplished at the present time. The cases herewith reported are successive* lobectomies performed for pulmonary tuberculosis. All had positive sputum. All were operated upon with a preoperative diagnosis of tuberculosis.

Discussion of total pneumonectomy in tuberculosis is intentionally omitted, despite a relatively large and favorable personal experience with this pro-

* One other case in which lower lobectomy was performed for bronchial stenosis following upper thoracoplasty has been intentionally omitted, although the patient is alive and well, with complete healing. The case illustrates different surgical principles. Grouping dissimilar cases creates the illusion of impressive numbers, but obscures important principles from which conclusions may be drawn.

cedure. It is quite another topic. The principles that introduce total pneumonectomy into the treatment of tuberculosis are totally different from those that underlie lobectomy. At the present time, total pneumonectomy cannot be considered an alternative to collapse therapy *provided that collapse*

FIG. 1b.—Section of the resected right lower lobe. Well encapsulated caseous mass. No bronchial communication demonstrable.

therapy is applicable to the case under consideration. It is both irreversible and nonselective. It irrevocably and seriously limits any therapeutic procedure that may be needed for the lung of the contralateral side. Circumscribed by strict indications, total pneumonectomy in tuberculosis may be a life-saving operation when no other procedure is feasible.

Lobectomy, on the other hand, is proposed as a *highly selective measure* for dealing with certain unilobar lesions. It is, indeed, far more conservative

of pulmonary function than even a seven rib thoracoplasty. Whether or no it is more selective than a skilfully controlled artificial pneumothorax is open to debate. Properly used, artificial pneumothorax has the advantage of being a reversible form of therapy. The therapeutic goal is a re-expanded healed lung. As lobectomy is by definition irreversible, it can be suggested as an alternate to artificial pneumothorax only when tuber-

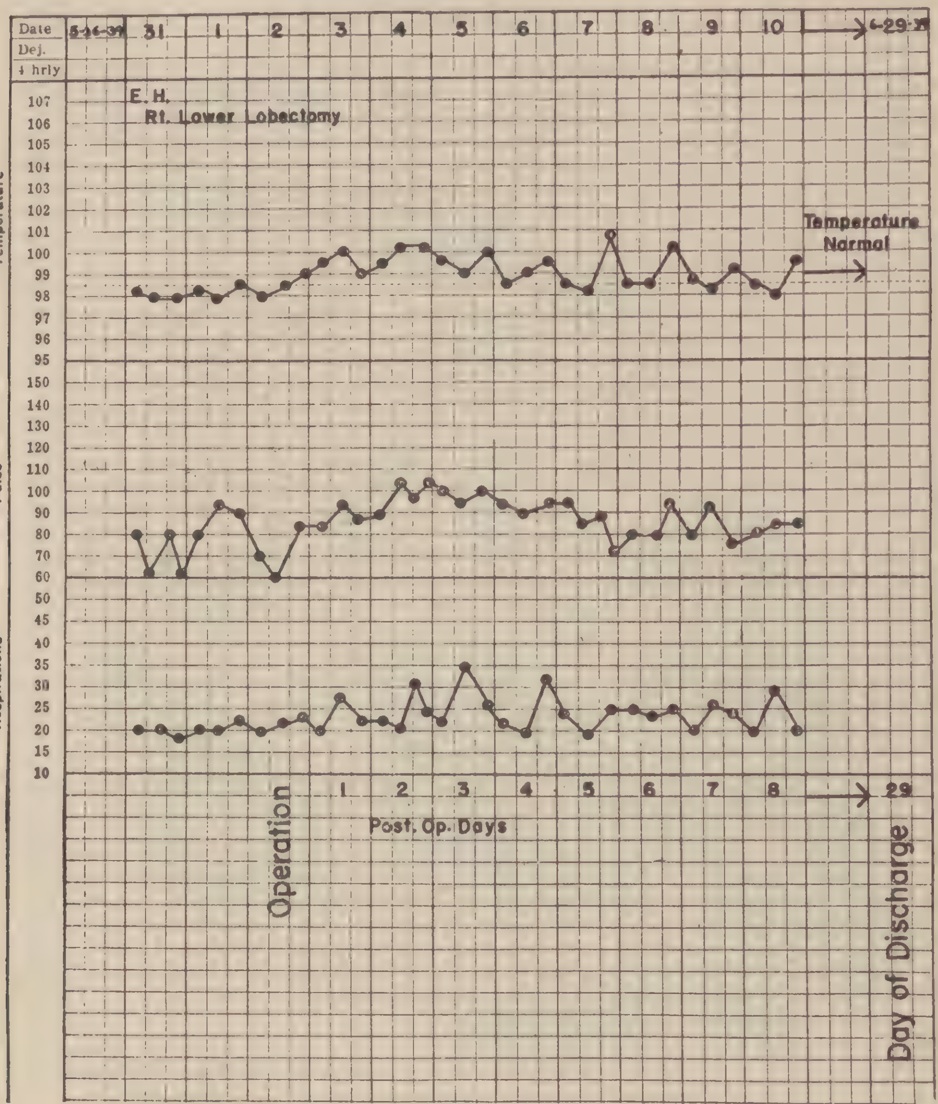


FIG. 1C.—Postoperative chart.

culosis has produced *irreversible* or *irreparable* destruction of lung substance. In these instances the strategy of a temporary reversible measure such as artificial pneumothorax is lost in the dilemma of either maintaining the collapse indefinitely, or facing reactivation by withdrawal.

The first three case records stand as instances of indications for lobectomy that can hardly be challenged as a departure from accepted surgical and

pathologic reasoning. Cases 4, 5 and 6, however, carry the matter further. Here, orthodox indications for thoracoplasty were disregarded, and a deliberate election of lobectomy substituted. Operation having been successful, it must be granted that *in these individual patients* lobectomy was preferable to thoracoplasty. The only question remaining is how frequently can such satisfactory results be achieved in a series large enough to be statistically significant. This can only be answered by further experience.

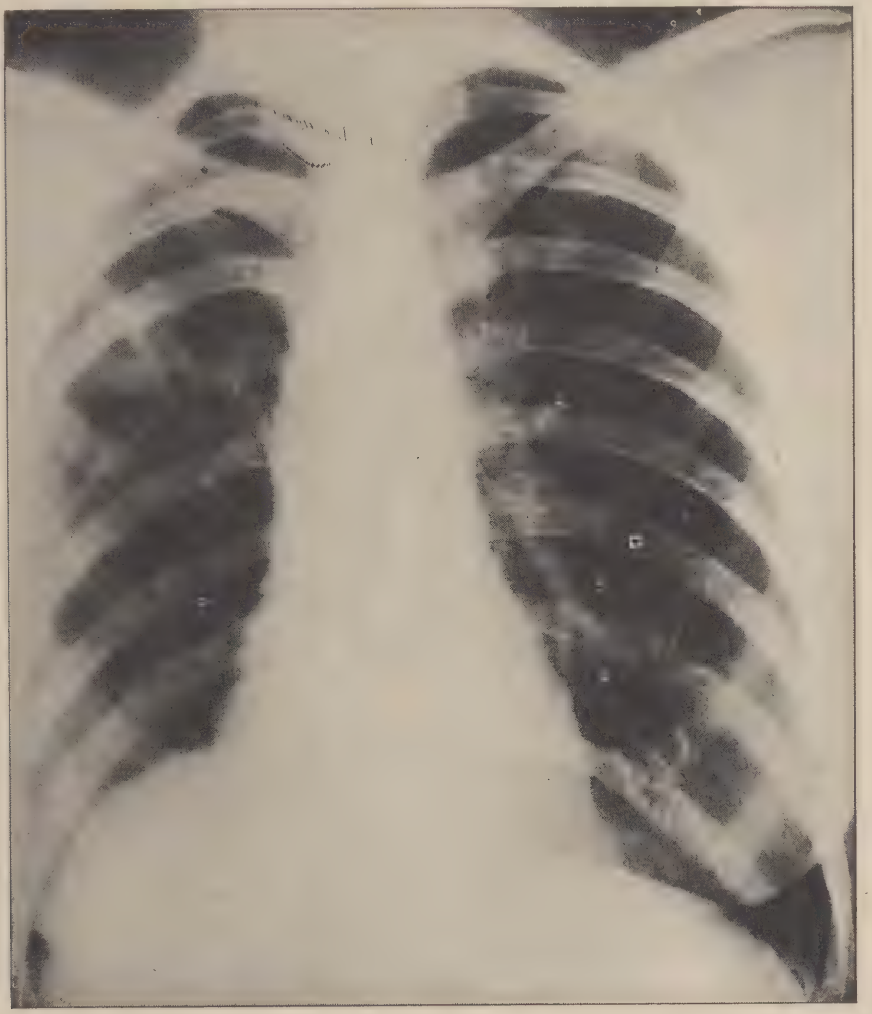


FIG. 1d.—Three years postoperative. The shadow beneath the 5th rib is not intrapulmonary but an opacity in the posterior pleura, continuous with the regenerated rib.

CASE REPORTS

Case 1.—U No. 194756: E. H., female, age 38 when she entered the Massachusetts General Hospital in May, 1939. She reported a run-down condition of 10 to 15 years' duration with increased susceptibility to respiratory infections. A "cold" in January, 1938, left a persistent cough. Roentgenograms and physical examination of the chest revealed an infiltration in the apex of the right lower lobe. *Sputum was positive for tuberculosis* in March, 1938. She entered a Saranac Lake sanatorium, where the sputum became "negative" in August, 1938, and remained so. The recovery seemed very satisfactory, although the area of density in the right hilum gradually increased

in size and showed a cavity in the center. Bronchoscopy and the bronchogram were uninformative. Several physicians considered that the appearance of the lesion was atypical for tuberculosis. Both malignancy and chronic lung abscess were considered.

On entry to this hospital the patient was essentially free of symptoms, her sputum was minimal in amount, and negative. The roentgenologist described an oval mass in the apex of the right lower lobe in contact with 6th and 7th dorsal vertebrae, measuring 6.5 x 4.5 cm. in diameter. An irregular cavity, with possible fluid level, was present in the mass. The periphery of the mass was smooth. There was definite thickening of the pleura overlying the vertebrae. The left lung was clear. The findings were considered consistent with tuberculosis, although admittedly unusual (Fig. 1a).

FIG. 2a.—Preoperative, November, 1941: Partially collapsed right upper lobe.

Operation.—6-2-39: Resection of the right lower lobe, with individual ligation technic.

Pathologic Examination.—In the apex of the right lower lobe was a caseous mass, well encapsulated, containing an irregular cavity (Fig. 1b). No free bronchial communication. A few scattered foci, pleural and subpleural, were present. *Smear from caseous material was loaded with acid-fast bacilli.*

Postoperative Course.—Uneventful. Patient was discharged on the 29th postoperative day in good health (Fig. 1c). She has been well since.

Postoperative Roentgenologic Examination.—June, 1942, three years after operation, negative for tuberculosis. Pleural scar in region of the 2nd rib (Fig. 1d).

COMMENT: This case represents the well known problem of the hilar round shadow, with or without cavitation. The majority of these are

found in the apex of the lower lobe. The "hilar" tuberculous lesion is the stepchild of surgical collapse therapy; disappointing results are likely to be obtained with any or all forms of treatment. Single foci in this location are usually hematogenous in origin without further tuberculous changes in the lung except for discrete, subpleural seeding in the same lobe. The latter

FIG. 2b.—Surgical specimen. The bronchi show a coarsely granular mucosal surface, particularly evident in the axillary branch. Microscopic changes throughout.

is a characteristic part of the pathologic pattern designated as "hematogenous." Massive foci are either the rather common "early round infiltration" with liquefaction that progresses slowly, or the so-called "punched-out" cavities, which are likely to be blocked and converted into a single caseous round focus. They closely resemble tumors, and are occasionally mistaken for lung abscesses. The findings in the present case are consistent with an early round infiltration in the state of protracted liquefaction.

Case 2.—U No. 329952: A. P., male, age 38, was admitted to the Massachusetts General Hospital in November, 1941. His previous history revealed that one and one-half years before entry, on a routine roentgenologic examination, a dense and contracted right upper lobe was found. Both sputum and gastric contents were *positive* for tuberculosis. At the Sanatorium of the Metropolitan Life Insurance Co., the patient was treated by bed-rest. A bronchoscopy revealed obstruction of the right upper lobe bronchus by a lesion described as a tuberculous granuloma. The condition of the patient remained satisfactory but the roentgenologic findings did not change. The minimal

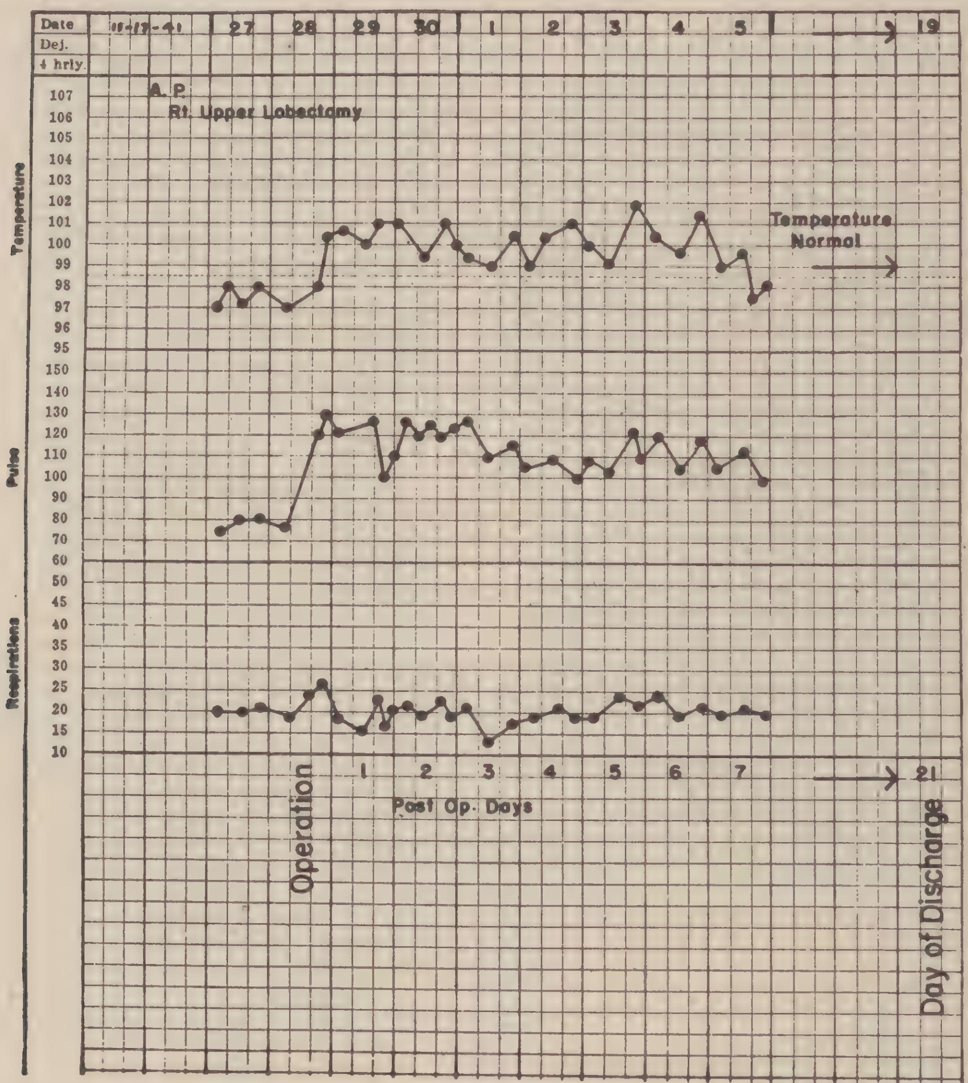


Fig. 2c.—Postoperative chart.

sputum continued to show tubercle bacilli. Surgery was advised, and the patient referred to the Massachusetts General Hospital. The physical examination, bronchoscopy and laboratory findings at this hospital confirmed the diagnosis of the Sanatorium. The interpretation of the chest film by our X-ray Department is as follows: "Partial collapse of the right upper lobe, with probable cavitation and stenosis of the right upper lobe bronchus" (Fig. 2a).

Operation.—11-28-41: Removal of the right upper lobe, with individual ligation technic.

Pathologic Examination.—Gross: A partially collapsed, anthracotic upper lobe, the pleural surface of which was smooth except for two small bands at the apex. Two major bronchi showed a coarsely granular mucosal surface, one a healed granuloma. There was no macroscopic parenchymal tuberculous lesion of any appreciable size. Those present were consistent with caseous bronchitis of the smaller and smallest bronchi. Scattered, grayish, small foci of fibrosis, some emphysema, numerous slightly dilated bronchi, some caseous, and some cystic in appearance made an impressive and characteristic pattern (Fig. 2b). *Microscopically,* studies revealed an almost uniform tuberculosis of the bronchial system of this lobe, although the tubercles were only to a moderate extent caseous, and subepithelial in location.

Postoperative Course.—Uneventful. The patient was discharged on the 21st postoperative day. (Fig. 2c).

Fig. 2d.—Postoperative, ten months (May, 1942).

Postoperative Roentgenologic Examination.—May, 1942: Shows no pathology beyond usual potsoperative changes. Lower lobe completely reëxpanded. The elevation of the diaphragm is due to crushing of the phrenic nerve (Fig. 2d).

Case 3.—U No. 360821: H. P., female, age 32, mother of one child, entered the Massachusetts General Hospital from the Rutland State Sanatorium in June, 1942. The patient had been well until May, 1941, when she developed a "cold" which persisted as a severe chronic cough. She was fluoroscoped in June and a "bronchial trouble" diagnosed. In July, 1941, she was admitted to a Worcester, Massachusetts Hospital because of severe cough accompanied by fever of 103° F. There she was treated for pneumonia, according to the patient's report. After discharge from that hospital she went to a physician who found tubercle bacilli in her sputum. She was referred to the Rutland State Sanatorium and admitted there. On admission the chest film revealed a process in the right upper lobe, which appeared decreased in size. In

the basal third of the right upper lobe was an homogeneous density with sharp marginal demarcation towards the lower and middle lobe (Fig. 3a). The findings were considered consistent with tuberculous infiltration, although collapse was recognized as a part of the pathology. The suspected tuberculous involvement of the right upper lobe bronchus could no be confirmed at that time. Artificial pneumothorax on the right side was instituted and maintained (Fig. 3b). The patient's symptomatic recovery was good, she gained twenty pounds, but her sputum continued to contain tubercle bacilli.

Operation.—7-9-42: The right 4th rib was resected and the right chest was opened. The lung was found collapsed due to the previous pneumothorax. When positive

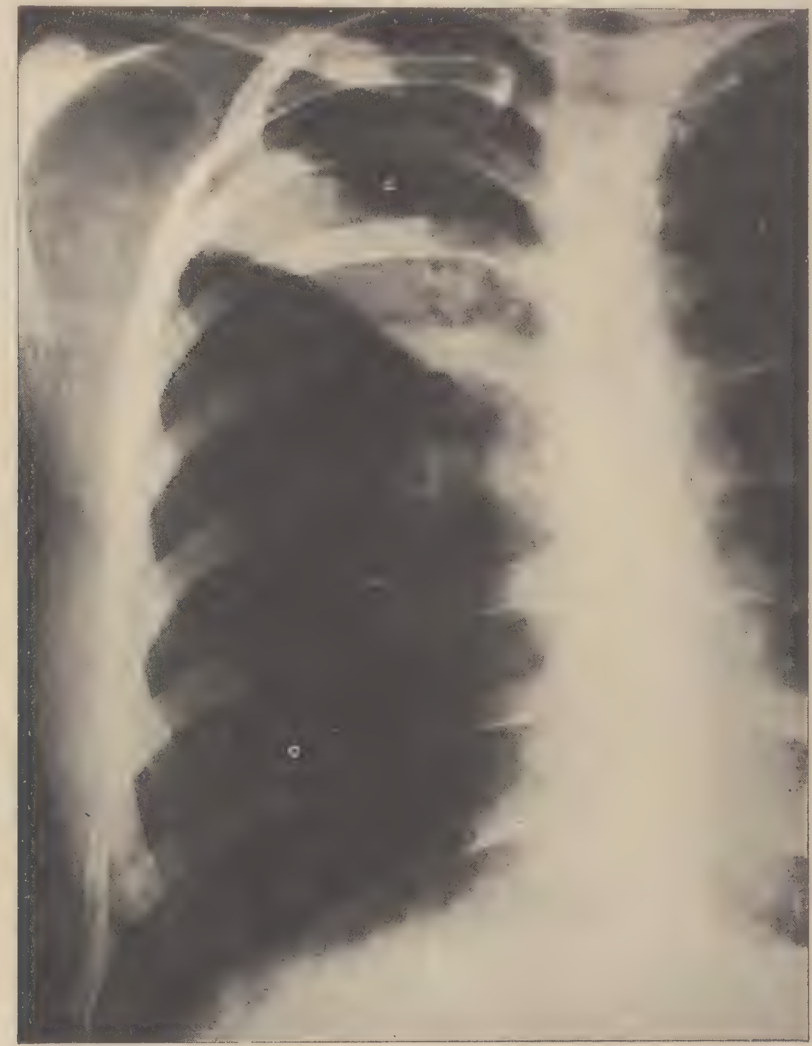


FIG. 3a.—On admission to the Rutland State Sanatorium, 1941. Right upper lobe decreased in size exhibiting an homogeneous density in the basal third.

pressure was applied the two lower lobes, *i.e.*, the middle and lower lobes, they expanded well but it was impossible to demonstrate any aeration of the upper lobe. A clamp was placed on the visceral pleura of the upper lobe to be used for traction purposes, and, from above downward, the lobe was dissected free from mediastinum and azygos vein where it was densely adherent. The structures at the hilum were isolated singly and the vessels doubly ligated. The lobe was then freed from the middle lobe. The ascending artery was identified and doubly ligated. The bronchus to the upper lobe was found to be partially stenosed by scar. The bronchus was closed. Denuded areas, particu-

larly over the azygos vein, were covered with pleura and the wound closed without drainage after the middle and lower lobes were expanded. Only a small amount of blood was lost during the entire procedure.

Pathologic Examination.—Gross: A Completely consolidated small right upper lobe. Upon section, the bronchi appear dilated and some of them coated with a thin caseous layer; others appear to be obliterated. No cavitation or scarring referable to previous excavation could be seen. In a small area there was a localized miliary caseation. This appeared, microscopically, as an interstitial seeding (Fig. 3c). *Microscopically,* the histologic appearance of the tuberculous lesions was exactly similar in character to that of the preceding case, although this lobe showed more extensive pathology. The lesions

FIG. 3b.—Preoperative film. This roentgenogram is identical in appearance with one taken two days after the induction of artificial pneumothorax.

were confined to the bronchi and bronchioles. Large areas of fibrosis and atelectasis were present. At the base, posteriorly, a recrudescent Ghon focus could be seen. The hilum in the region of dissection was free of tuberculous nodes. The peribronchial lymph nodes contained small caseous foci.

Postoperative Course.—Uneventful. The patient was discharged on the 22nd day (Fig. 3d).

Postoperative Roentgenologic Examination.—Shows the condition August 3, 1942, four weeks after operation. Some apical fluid or apical thickening of the pleura is still present (Fig. 3e) although the Rutland State Sanatorium reported good breath sounds all over the chest at that time. On February 1, 1943, she is reported to be in perfect health, with fluoroscopic findings normal except for paralysis of the right diaphragm.

COMMENT: Cases 2 and 3 exhibit the peculiar pathologic pattern of unilobar tuberculous involvement of the bronchi, large and small. As to pathogenesis, an hematogenous origin is the most probable. Aspiration as the cause of this caseous bronchitis appears out of question, since there is no liquefying focus or chronic cavity to provide so thorough a seeding. Unilobar caseous bronchitis is likely to be erroneously considered as an infiltrative or exudative lesion due to the dense homogeneous roentgenologic appearance and sharp marginal demarcation. The third case (H.P.) demonstrates better than any statement the effect of collapse therapy upon a lobe the bronchi of which are diseased. The induction of the pneumothorax was followed by an immediate and complete collapse, giving in two days an appearance identical

FIG. 3C.—Surgical specimen. Cut surface of the resected lobe. See the note on the pathology of this specimen.

to the film reproduced in Figure 3b. Such an occurrence in the early phase of pneumothorax therapy should be regarded as an indication that one is not dealing with an infiltrative process which can be successfully treated by collapse therapy. This type of underlying pathology leads to the complication of the unexpandable lung. Even the most ideal and long standing collapse may not lead to healing of the tuberculous process if there has been an incorrect interpretation of the pathology. Thoracoplasty would have been equally ineffective. Ablation of the involved lobe seems the only feasible form of therapy.

Case 4.—U No. 345056: L. F., female, age 22, was admitted in March, 1942, from the Rutland State Sanatorium. Her disease was discovered in October, 1941, by a routine roentgenologic examination following a diagnosis of pulmonary tuberculosis made on her brother one month earlier. She was found to have an indurative tuberculosis, with cavitation in the right upper lobe, and positive sputum. She was admitted immediately to the Rutland State Sanatorium. Therapeutic pneumothorax could not be established because of obliteration of the pleural space, therefore, she was kept on bed-

rest for six months. On admission to the Massachusetts General Hospital the patient was in excellent condition. A roentgenogram showed mottled dullness in the right first interspace and the right apex. Within the mottling in the first interspace there was a cavity 2.5 cm. in diameter, lying in the posterolateral aspect of the lobe. This film showed essentially the same condition that had existed on admission to the Rutland State Sanatorium (Fig. 4a).

Operation.—4-27-42: Right upper lobectomy. Adherent and obliterated pleural space

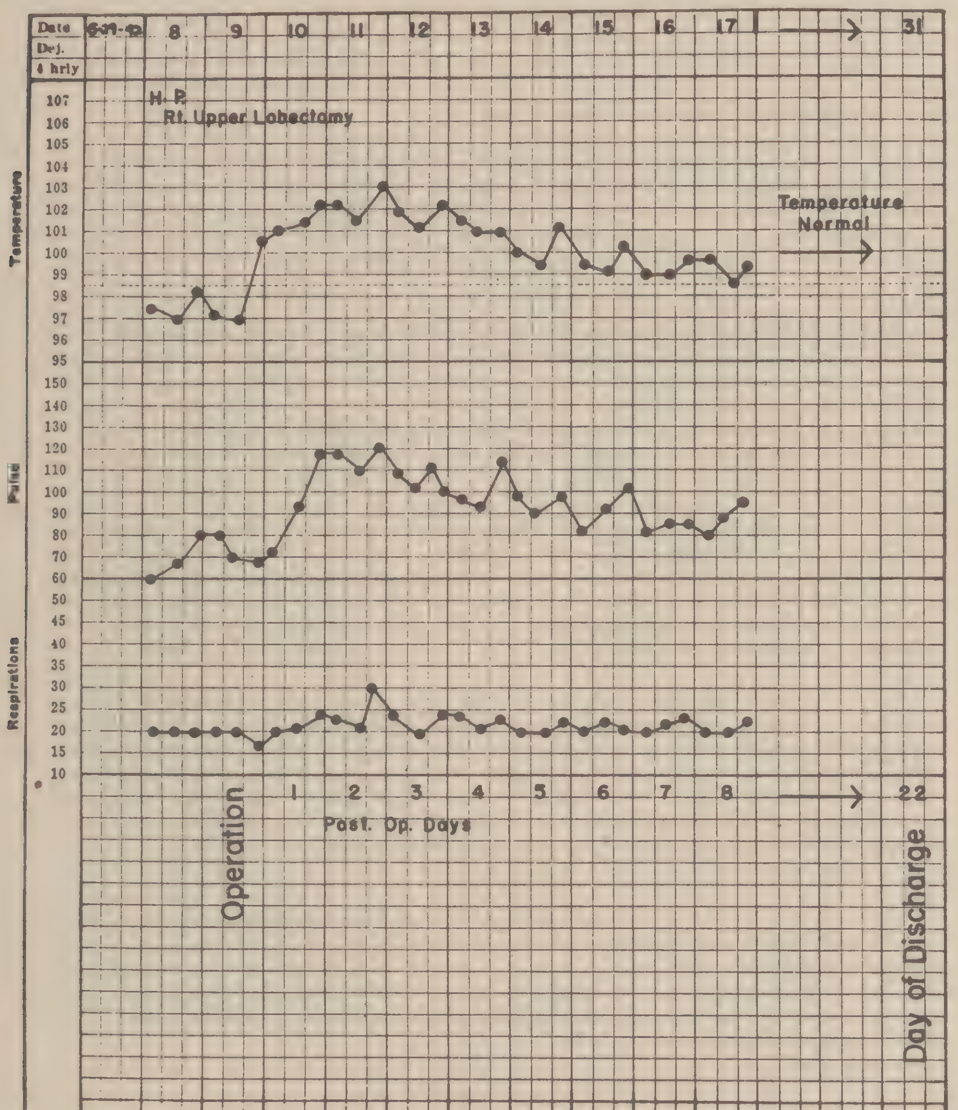


Fig. 3d.—Postoperative chart.

developed by resection of the 4th rib. Near the angle of the ribs in the lower portion of the upper lobe, the lung was densely adherent to the parietal pleura over the cavity. A patch of parietal pleura, approximately 3 cm. square, was excised to keep the plane of mobilization at a distance from the wall of the cavity.

The remainder of the parietal surface of the lobe was easily mobilized, although everywhere adherent. Considerable care was necessary in dividing the fissures, the one with the lower lobe being involved in the inflammatory reaction of the disease, and the anterior portion of the middle lobe fissure being anatomically very incomplete.

After these were developed the hilum was easy to dissect, ligating the superior branch of the pulmonary artery in two divisions and the superior pulmonary vein in three branches. No ascending upper lobe artery was identified. It was believed to be absent. The bronchus was isolated and secured with a catgut mattress suture. It was amputated at its first division and the end closed with interrupted silk after cauterizing the mucous membrane with phenol. No pedicle flap was available for coverage. The mediastinal pleura was sutured over it and, after crushing the phrenic nerve at the level of the azygos vein, the hilar portion of the lower and middle lobes could be drawn up to cover the bronchial stump.

The adhesions of the dorsal segment of the lower lobe to the parietal pleura were divided to allow its ascent toward the apex. The lower part of the pleural cavity was

FIG. 3e.—Roentgenogram of the chest four weeks after operation (August 3, 1942). No tuberculous pathology visible.

found completely obliterated. The pleural space was dusted with four grams of sulfanilamide, and the incision closed with silk, without drainage. Air was aspirated.

Pathologic Examination.—Gross: The specimen shows the posterior part of the right apex changed by radiating induration of rubber-like consistency. At the center lies a "punched out" cavity the inner surface of which is coated with a very thin caseous exudate. A small bronchus, the only one, leading toward the cavity is obliterated. The superior and anterior part of the apex exhibits an irregular gray scar intermixed with emphysematous parenchyma representing a healed lesion of earlier date (Fig. 4b).

Postoperative Course.—This was, as in preceding cases, extremely smooth and uneventful. She was discharged on the 35th postoperative day (Fig. 4c). One month after operation tuberculin tests (1:50,000 and 1:20,000 O.T.) were negative. She is living with her family at home.

Postoperative Roentgenologic Examination.—July, 1942: Showed no pathology except usual postoperative changes (Fig. 4d).

COMMENT: This patient was deliberately chosen, with her consent, for lobectomy as preferable to a thoracoplasty. Artificial pneumothorax was impossible.

Case 5.—U No. 373702: E. S., female, age 22, was admitted to the Massachusetts General Hospital in September, 1942, from the Channing Home. She had entered the Channing Home in August, 1941, with a history of fatigue and cough of six months' duration. A roentgenogram of her chest at that time showed a cirrhotic process with large multiple cavitations in the right upper lobe and two small liquefied aspiration

FIG. 4a.—Roentgenogram on admission to sanatorium, same as preoperative film, taken six months later. In the right first interspace mottled dullness with cavitation, 2.5 cm. in diameter.

foci in the left midlung field (Fig. 5a). Sputum was strongly positive. In September, 1941, a right pneumothorax was instituted but was abandoned shortly thereafter because of numerous adhesions. In December, 1941, a pneumothorax on the left side was started but discontinued because of gastric distress. In January, 1942, a right temporary phrenic paralysis was induced. She continued to improve in the Channing Home but in April, 1942, she had a small hemoptysis. Temperature reached a maximum of 99.4° F. The sputum remained strongly positive.

On admission to the Massachusetts General Hospital for surgery her general condition was good. A roentgenogram showed essentially the same process as at entry to the Channing Home. The right upper lobe was, in its larger portion, destroyed by cavitation. The remaining parenchyma of the lobe appeared dense.

The left lung was apparently stable but there was a suggestion of a one cm. cavity with some infiltration around it in the mid-lung field, where the cavitation had been demonstrated previously (Fig. 5b). The sputum was loaded with tubercle bacilli. Bronchoscopy was uninformative.

Operation: A right upper lobectomy was performed on September 16, 1942. Under intratracheal gas-oxygen-ether anesthesia with the patient lying on her left side, the right chest was prepared with iodine and an incision made over the 5th rib. The muscles were divided down to the chest wall. Subperiosteal resection of the 5th rib was done. The pleural cavity was opened through an area free of adhesions, and it was then seen that the right upper lobe was densely bound down by adhesions. An

FIG. 4b.—Surgical specimen. The photograph shows only the diseased area. Note the sclerotic tissue surrounding the cavity.

intrapleural dissection was started and continued until it was found that bleeding was excessive in this plane. Extrapleural dissection was then attempted and found to be more feasible. By combined intra- and extrapleural dissection the upper lobe was entirely freed, bleeding vessels being controlled with dura clips and silk ligatures. The fissure between the middle and lower lobes of the lung was found to be free of adhesions. Following the individual ligation of the pulmonary veins and arteries, the bronchus was isolated, closed with a mattress suture, and cut across. Several sutures were placed to close the bronchus. During the entire procedure there was no contamination of the pleural space nor was the lung tissue opened. The middle lobe was freed so that the end of it could be sutured over the closed bronchus. Four grams of sulfanilamide were dusted into the pleural cavity after hemostasis was complete. The lower lobe was

entirely mobilized to make expansion of that portion of the lung more complete postoperatively. The chest was closed in layers with multiple interrupted silk sutures. The skin was closed with silk. No drainage.

Pathologic Examination.—A small sclerotic right upper lobe. It is almost completely excavated presenting a large cavity over an area 6 x 8 cm. The excavation extends immediately beneath the pleura and presents a rigid wall surrounded by firm

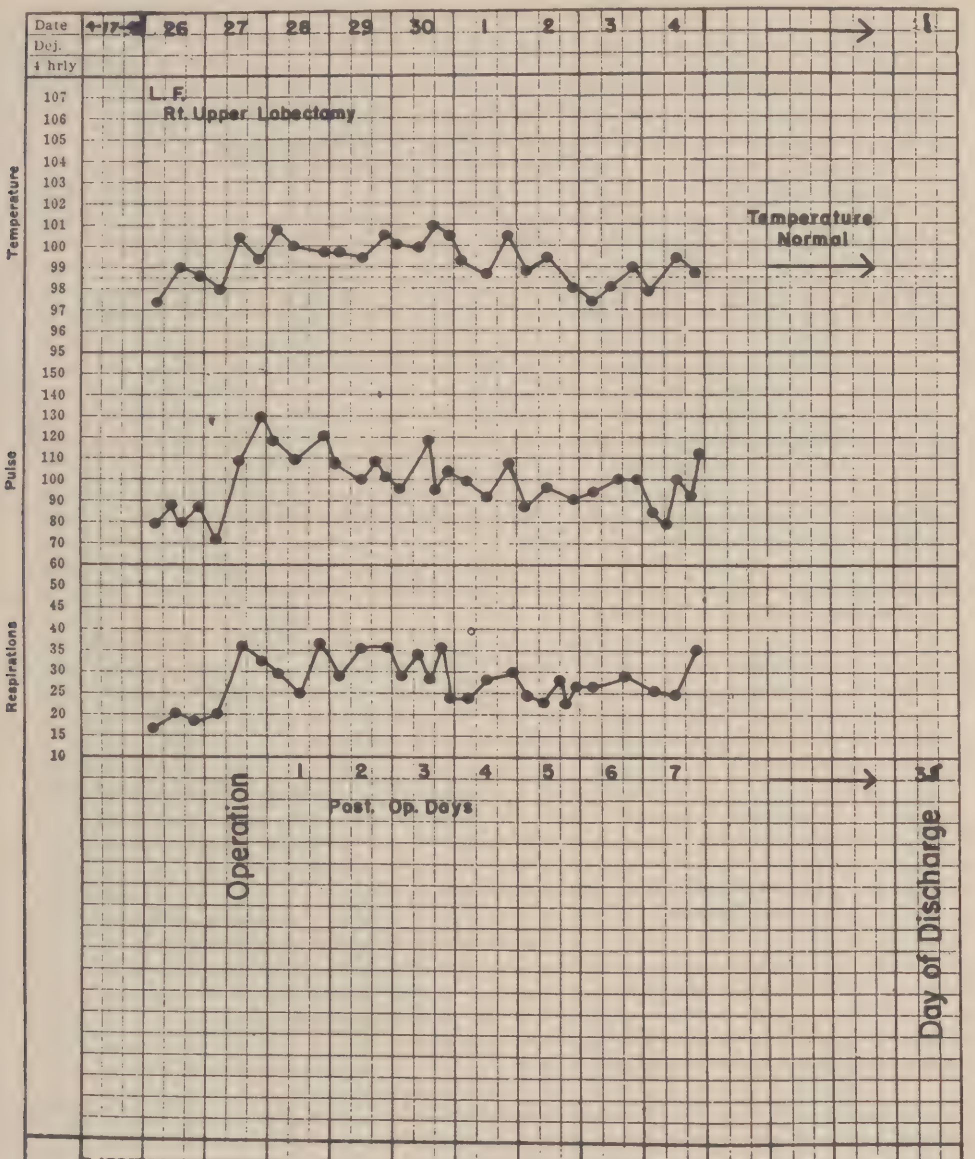


FIG. 4c.—Postoperative chart.

induration. The inner wall of the cavity is coated by a heavy caseous lining and affords only one small communication with the bronchial tree. The rest of the lobe is completely airless and does not show active tuberculous foci. At the very apex there is a layer of fibrous tissue representing extrapleural surgical resection (Fig. 5c).

Postoperative Course.—Uneventful. Patient had no cough and no expectoration whatsoever. Discharged on the 23rd day (Fig. 5d). Preoperative and postoperative tuberculin skin tests showed a sensitivity 1:50,000.

Postoperative Roentgenologic Examination.—December 11, 1942: Showed on the

right side no pathology, other than postoperative changes. The lesion on the left was resolved except for a 1.5 cm. thin wall ring shadow (Fig. 5e). Since the main lesion had been eradicated, the control of the contralateral cavity by pneumothorax became a hopeful therapeutic measure. Accordingly, on December 16, 1942, left pneumothorax was re-established and has been continued (Fig. 5f). In March, 1943, sputum was still positive, and bronchoscopic examination showed no evidence of ulceration or tuberculous granulation in any of the bronchi.

FIG. 4d.—Postoperative three months (July, 1942). No tuberculous pathology visible.

COMMENT: The case presents the rather crucial problem of contralateral disease in the presence of a giant upper lobe cavity in a young woman, age 24. The contralateral side had exhibited susceptibility to bronchogenic spread and contained two small cavities. Pneumothorax had proved to be ineffective. In accord with usual practice, thoracoplasty would be the method of treatment. Considering the extent of the disease, several stages would have been required to close this cavity and the tiny bronchial communication may well have produced the "block" phenomenon. During the entire course of the surgical program the dangers of bronchogenic aspiration spread would have persisted.

The selective nature of lobectomy is well illustrated in that the chief focus of the disease was eliminated by a single operative procedure that

Fig. 5a.

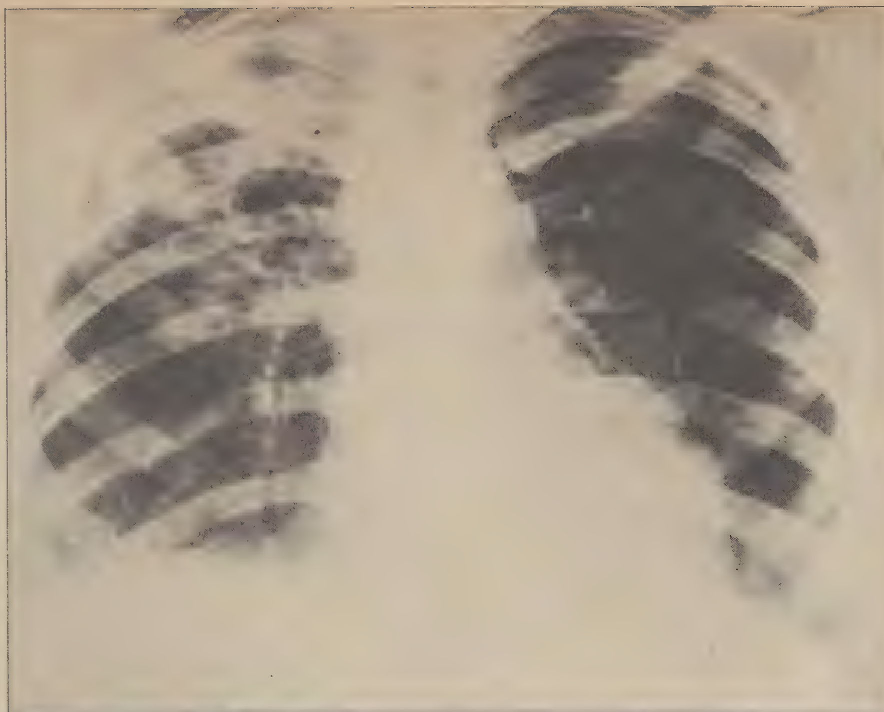


Fig. 5b.

Fig. 5a.—August, 1941. Cirrhotic tuberculosis, with extensive cavitation in the right upper lobe. Left midlung field shows two cavities, representing liquefied aspiration foci.

Fig. 5b.—On admission to the Massachusetts General Hospital. The cavities in the right upper lobe enlarged. Lesion on the left side unchanged but obscured by perifocal infiltration.

left the right lower and middle lobes intact. It was then possible to institute a contralateral artificial pneumothorax for the preexisting bronchogenic spread.

Case 6.—U No. 377199: M. M., female, age 35, was admitted in October, 1942, to the Massachusetts General Hospital. Her first breakdown was 13 years previously—treated with bed rest for two years. Sputum was negative at that time. In 1936, tuberculosis flared up in the left upper lobe. According to the available roentgenogram (Fig. 6a) she had a productive tuberculosis in the left upper lobe with a few circum-

Fig. 5c.—Surgical specimen. Note the size of the cavities, their sclerotic walls and the lack of bronchial drainage with the exception of a single "pin head"-size communication with the bronchial tree. There was no reason to predict that a "blocked" cavity existed.

scribed foci but without visible cavitation. The sputum became positive at that time. She was treated with artificial pneumothorax on the left side (Fig. 6b). The treatment was continued for three and one-half years. After reexpansion she was able to lead a normal and active life. In June, 1942, she developed a productive cough. The sputum became *positive* for tubercle bacilli. In July, 1942, she was concerned with marital worries and difficulties and lost 14 pounds of weight. A roentgenogram, however, did not show any change as compared with the one taken after her pneumothorax was discontinued. At that time she also complained of fatigue. She was readmitted to the Channing Home where the pneumothorax had been originally started. The staff of this institution referred the patient for surgery.

On admission to the Massachusetts General Hospital the patient was in good general

condition. The sputum was minimal but contained tubercle bacilli. A roentgenogram (Fig. 6c) showed a shrunken and dense upper lobe on the left side, with scattered, circumscribed foci, varying in size from 2 to 5 mm. in diameter. No cavity was visible.

Operation.—10-14-42: A left upper lobectomy was performed. With the patient under intratracheal gas-oxygen-ether anesthesia, and on her right side, the left chest was prepared with iodine. An incision was made over the course of the 5th rib and curved in order to free the tip of the scapula. The trapezius was divided posteriorly, then the rhomboids and serratus posticus identified. This was separated from its attachment to the 5th rib and suberiosteal resection of the rib carried out. The pleural cavity was entered. Dissection of the left upper lobe was then carried out through very tenuous, avascular adhesions. Sharp dissection was necessary throughout. The

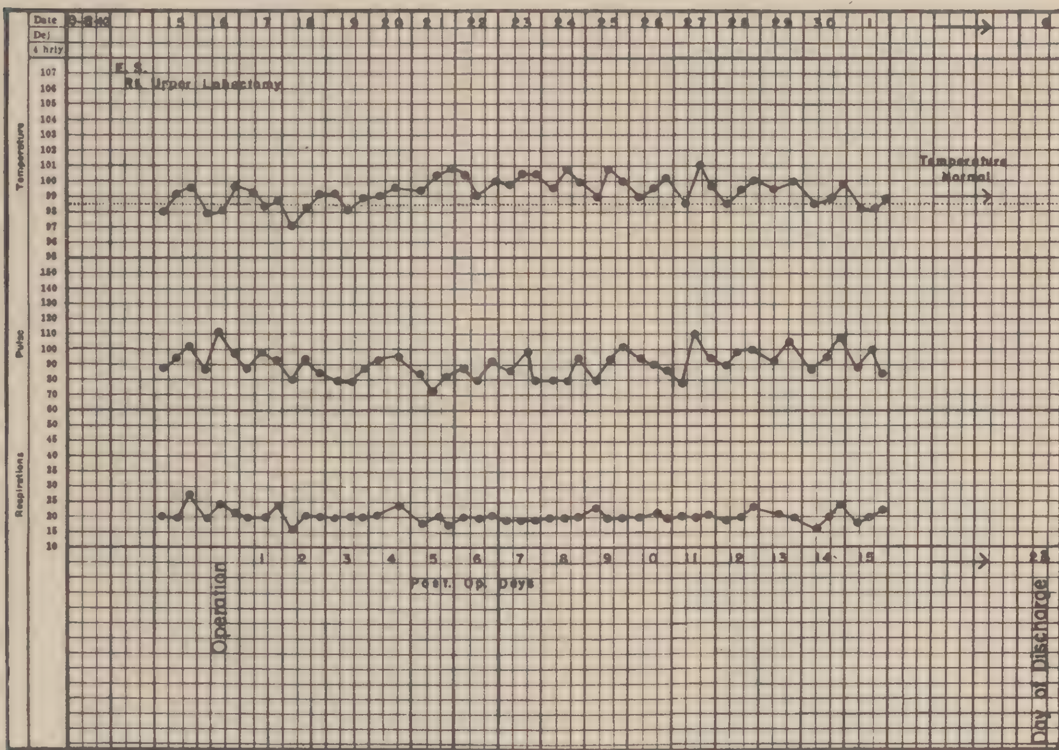


Fig. 5d.—Postoperative chart.

fissure between the lower and upper lobes of the left lung was identified and developed. On the posterior upper aspect of the lobe, considerable difficulty was met in freeing the lung from adhesions. The hilum of the lung was approached and individual ligation of the arteries and veins carried out. The fissure between the upper and lower lobes was then completed by cutting between clamps and suturing the defect. The bronchus to the left upper lobe was identified, two stay-sutures inserted and the bronchus divided. The bronchus was then closed with multiple interrupted silk sutures. The left lower lobe was then partially mobilized and a pedicle sutured over the closed bronchus. The specimen removed contained left upper lobe and lingula. Four grams of sulfanilamide were dusted into the pleural cavity, and the chest closed in layers, the divided muscles and skin being approximated with silk. The patient left the operating room in good condition, blood pressure being 110/80, and her blood well oxygenated.

Pathologic Examination.—Gross: (Fig. 6d): A shrunken left upper lobe. The pleural surface is roughened by the presence of fibrous tags representing old adhesions. The major bronchi have thickened walls and narrowed lumens. At the very apex there are several foci which hold inspissated caseou débris, and have sharply defined walls. They represent either previous cavities or old round foci, the latter are the

FIG. 5e.

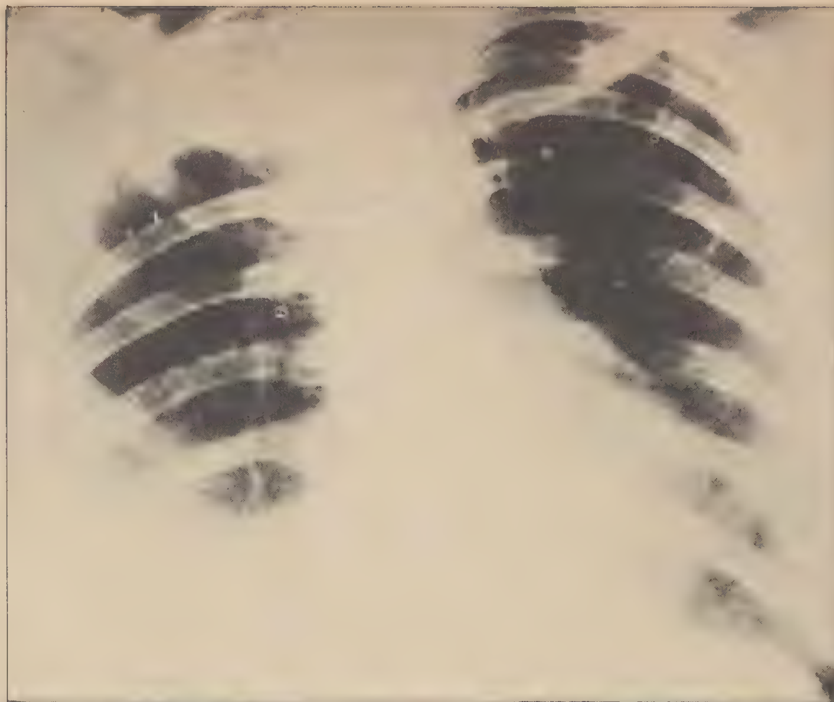


FIG. 5f.

FIG. 5e. (Above)—Postoperative eight weeks (December 11, 1942): The right side is without visible tuberculous pathology. The left side exhibits two thin-walled small cavities, without the perifocal infiltration seen in the immediately preoperative film. No signs of postoperative exacerbation.

FIG. 5f. (Below)—Postoperative roentgenogram (December 30, 1942): Marginal artificial pneumothorax induced on left. Cavities no longer visible.

more probable. In the midportion of the lobe a few more foci are seen, the contents of which are caseous and firm. These, too, are well encapsulated but one presents a possible caseous breaking within the capsule. At the base of the lobe linear caseous stripes are seen representing traces of caseous bronchitis. The upper part of the lobe contains considerable fibrosis; the lower part is partially atelectatic. Both the distribution and the morphology of the caseous foci and the clinical course suggest very strongly an hematogenous origin of the process.

Postoperative Course.—Postoperative course was uneventful except that the patient

Fig. 6a.—May, 1936: Productive well circumscribed foci, no visible cavitation. Sputum positive for tuberculosis. Pneumothorax induced.

developed a transient pleural effusion which resorbed again within a few weeks. Patient was discharged on the 30th postoperative day to the Channing Home (Fig. 6e).

Postoperative Roentgenologic Examination.—1-15-43: Showed a completely re-expanded left lower lobe, with a probable small effusion in the apex of the pleural space (Fig. 6f). Although the patient's general condition is good, her sputum has remained positive. Bronchoscopic examination on March 12, 1943, revealed narrowing and irregular proliferation of the left main bronchus with a 5 mm. ulceration.

Comment: The clinical significance of this case resides in the problem of cavity healing. Considering the complexity of questions and factors involved, the problem is proposed rather than discussed at this time. Cavity healing has been studied in recent years by Auerbach, Pagel, Pinner and others. According to these studies three anatomic forms of healed cavities can be differentiated: 1. The solid focus due to retention, inspissation, and final calcification of the cavity contents. 2. Radiating scar. 3. The bron-

chiectatic area remaining after the substitution of caseous and tuberculous elements in the cavity wall by ordinary granulation tissue, with subsequent epithelization and fibrous shrinking of the space. Healing by conversion of the cavity into a solid focus seems to be the most frequent form of cavity healing. It is noteworthy that the cases studied, the number of which is too small (16) to permit of a statistical analysis, were almost without exception obtained from individuals previously treated with some form of collapse therapy. In other words, collapse therapy, pneumothorax and thoracoplasty

FIG. 6b.—August, 1936: Incomplete artificial pneumothorax.

alike, may favor the conversion of the open cavity into a closed one that may still maintain a caseous focus.

We have been fortunate in being able to carry on careful studies on a relatively large number of surgically removed lobes and lungs. The specimens have all shown one type of cavity residuum, the so-called converted focus which, in clinical practice, is designated as "healed." These well walled-off foci, although firm in consistence, invariably contain caseous material. One or two in each specimen appear to be in the process of breaking through their capsules. It does not appear to be a permanent and safe method of cavity healing, yet it may well represent the characteristic response to collapse therapy.

The reliable type of cavity healing seems to be the concentric shrinking, with scarring. The two other types represent unrepaired damage to the lung, with a constant potentiality of reactivation or spread. These observations help explain the reluctance of the clinician to permit reexpansion of the lung after the disease appears to be under control with artificial pneumothorax. They also add weight to the proposal that irreparably damaged lobes be resected.

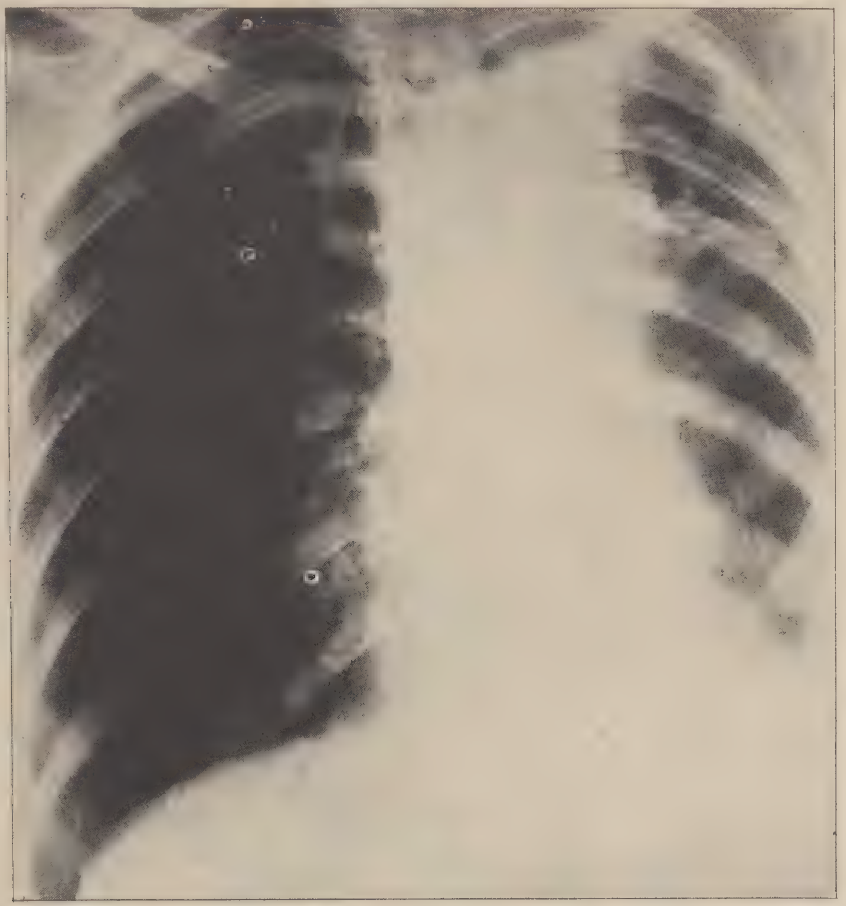


FIG. 6c.—Preoperative. The process present in the left upper lobe essentially unchanged compared with postpneumothorax roentgenograms, and with that from 1936.

TECHNICAL NOTES

Bronchoscopy: All patients were subjected to bronchoscopy preoperatively to rule out the presence of active ulceration in the trachea or stem bronchus.

Anesthesia: Gas-oxygen-ether administered through an intratracheal tube.

Incision: Posterolateral, with resection of a single rib at the appropriate level. An anteriorly placed incision would seem to impose unnecessary technical difficulties on the operator.

Dissection: In areas overlying densely adherent cavities the dissection is transferred from the intrapleural plane to the extrapleural plane. In looking for a fissure, however, one must be certain to return to the intrapleural plane. A layer of thickened parietal pleura will completely obscure the fissure. Meticulous hemostasis is maintained by ligatures and silver clips.

The frequently repeated statement that access to the hilum may be blocked by tuberculous infiltration of lymph nodes is erroneous. Once the primary lesion is established, tuberculous foci in an organ do not produce a lesion in the corresponding lymph nodes.[1] Upper (or lower) lobe lobectomy is carried out by individual ligation technic. An accurate knowledge of the complex anatomic structures and their common variations is essential.

FIG. 6d.—Surgical specimen. Note the morphology and distribution of the foci. Traces of caseous bronchitis. (Pattern of hematogenous pulmonary tuberculosis.)

Following upper lobe resection the lower lobe, if adherent, is mobilized so that it may ascend to fill the apex. Intrathoracic crushing of the phrenic nerve has been done to reduce temporarily the volume of the hemithorax. Whether this is necessary or even advisable remains to be seen. In thoracoplasty one fears lower lobe aspiration pneumonitis in the presence of a paralyzed diaphragm. With surgical ablation of the source of sputum and complete freedom from paradoxical motion of the chest wall the conditions are quite different.

Silk technic is used throughout except for a proximal row of sutures penetrating the bronchial mucosa, where fine chromic catgut has been employed.

The pleural cavity is closed without drainage and the chest wall muscles approximated by interrupted sutures of fine silk. Intrapleural pressure is adjusted to a moderate degree of negative pressure.

Postoperative Care: An oxygen tent is used routinely for the first 24

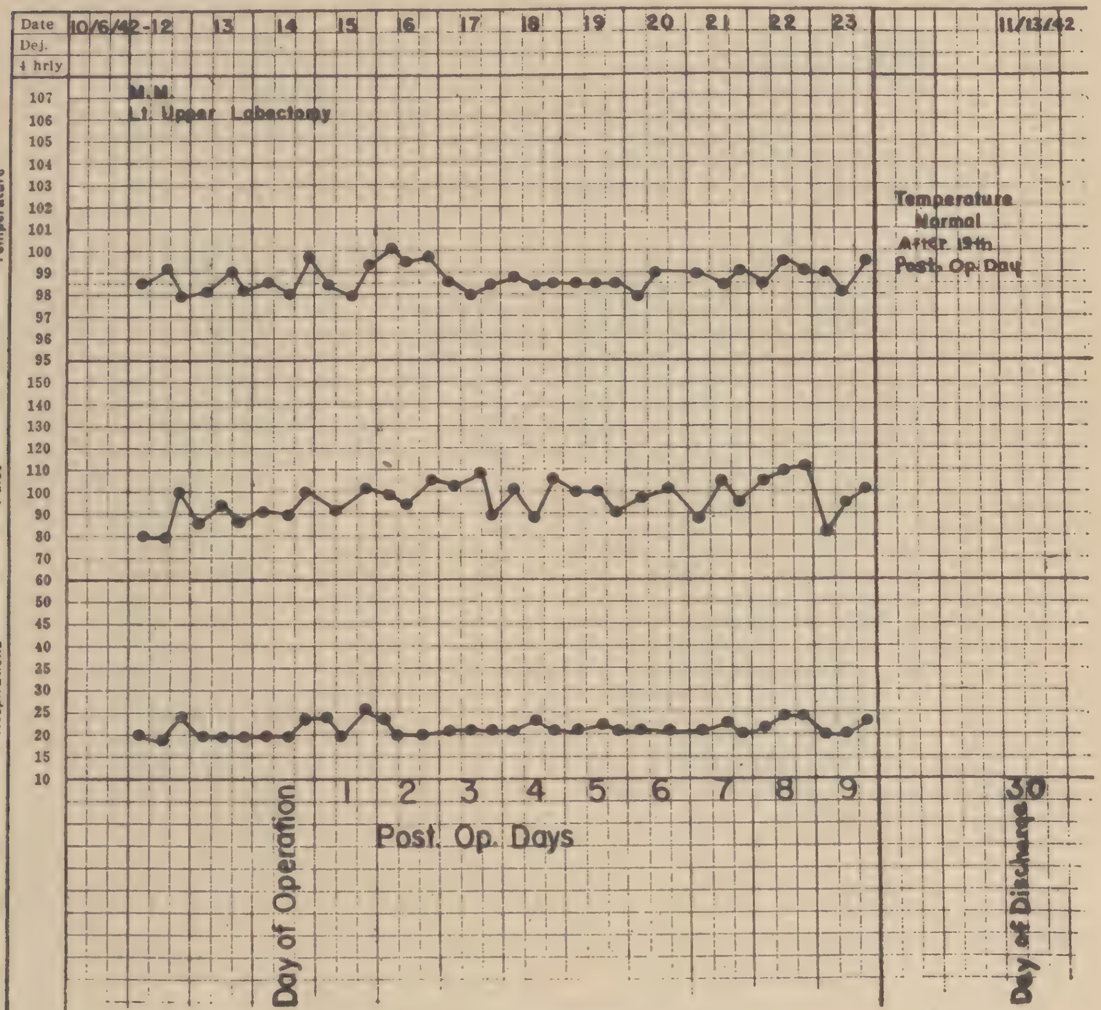


Fig. 6e.—Postoperative chart.

hours. Fluid or residual air may be reduced with needle aspiration, according to individual indications, preferably maintaining a moderate degree of negative pressure.

General Comments: *If a lobectomy has been planned, technical difficulties that lead to resection of the entire lung must not be countenanced.* The goal of the operation is conservation of normal lung tissue as well as ablation of the diseased focus. Interlobar fissures that have been obliterated by adhesions, or anatomically incomplete fissures, *can and must be developed* by careful dissection. Discovery of healed foci in adjacent lobes is not an indication for resecting them.

From a technical standpoint total pneumonectomy is a more rapid and simple procedure than individual ligation lobectomy. Obviously, it has no place in this discussion as an alternative to artificial pneumothorax or thoracoplasty in dealing with unilobar tuberculosis.

Discussion: Collapse therapy is eminently satisfactory in a high percentage of cases of pulmonary tuberculosis that require radical therapy. Its hazards are computable and by no means excessive. It has lightened but not eliminated the great economic and temporal wastage of the disease.

Fig. 6f.—Postoperative, January 15, 1943, three months after left upper lobectomy. There is one large and a few small calcifying foci visible in the apex of the reexpanded lower lobe but no active pathology discernible.

It may, for an indefinite period, remain the best form of treatment for the vast majority of patients requiring surgical intervention.

Before factual data are at hand to establish the safety of lobectomy as contrasted with thoracoplasty or long-continued artificial pneumothorax, it may seem mischievous to speculate regarding the theoretic advantages of such a procedure. A shortening of the span of treatment is not the least of these. Conversion of the personality all too frequently accompanies conversion of the sputum when the latter is attained at the expense of years of invalidism.

But from the more concrete physical point of view there are certain things to be gained. Lobectomy is more highly selective than thoracoplasty and as selective as the most skillfully managed pneumothorax, assuming in the

latter instance that healing and reexpansion are prohibited by the actual pathology. The functional capacity of the remaining lobe, or lobes, in the diseased side is preserved rather than encroached upon by long continued artificial pneumothorax or thoracoplasty.* The anatomic integrity of the thoracic cage and shoulder girdle remains essentially intact.

Most important of all, however, is the immediate ablation of the offending lesion in its entirety. This does not mean, of course, that the disease, tuberculosis, can be totally excised in many instances. While the open lesion under attack may represent only one manifestation of a generalized disease, there is reason to believe that its removal may aid rather than deleteriously affect remote latent or quiescent foci.

Surgeons familiar with tuberculosis will not need to be reminded that resection can only be considered after the patient's immunologic equilibrium has been restored by rest under a sanatorium regimen. Empyema, bronchial fistula, and implantation in the incision may otherwise be expected.

Artificial pneumothorax is in no way incompatible with subsequent lobectomy. When bed-rest alone is insufficient to bring the disease under control, pneumothorax or phrenic nerve paralysis may be added. If there is good reason to believe that the therapeutic goal of a reexpanded lung, with a closed lesion, cannot be achieved within a reasonable length of time, lobectomy may be considered when the acute phase has been brought under control.

CONCLUSIONS

Six cases of pulmonary tuberculosis are presented, three of which provided orthodox indications for resection of the lesion by lobectomy. Three others presented the usual indications for thoracoplasty but lobectomy was performed by election.

Healing *per primam* was the result in all instances.

Lobectomy provides a more selective and immediate method of eradicating certain lesions of tuberculosis than does collapse therapy. It may be used subsequent to artificial pneumothorax, thereby restoring to that procedure the reputation of finesse that it should enjoy.

A method of treatment that combines conservation of lung function, with immediate conversion of the sputum, and a shortening of the span of treatment, cannot be dismissed until its scope has been more fully explored.

REFERENCES

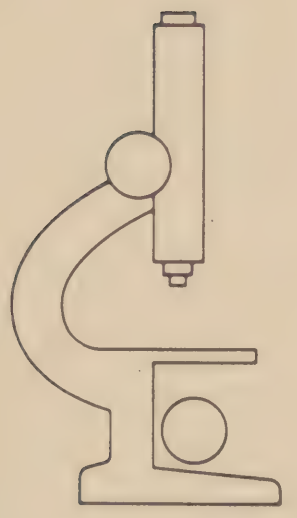
[1] Kayne, George Gregory, Pagel, Walter, and O'Shaugnessy, Laurence: Pulmonary Tuberculosis: Pathology, Diagnosis, Management and Prevention. Oxford University Press, London, New York, Toronto, 1939.

[2] Kent, Edward M., and Blades, Brian: The Surgical Anatomy of the Pulmonary Lobes. Jour. Thor. Surg., **12**, 18, October, 1942.

[3] Thornton, T. F., Jr., and Adams, W. E.: The Resection of Lung Tissue for Pulmonary Tuberculosis. Surg. Gynec. & Obst., **75**, 312, October, 1942.

* The apex of the lower lobe lies at the level of the fourth rib in the paravertebral gutter. Modern "apical" or "selective" thoracoplasties rarely spare the sixth rib, and usually extend to include the seventh.

notes



EXPERIMENTAL THERAPY

EVALUATION OF CHEMOTHERAPEUTIC AGENTS IN CLINICAL TUBERCULOSIS[1]

A Suggested Procedure

H. CORWIN HINSHAW[2] AND WILLIAM H. FELDMAN[3]

The recently acquired knowledge that certain drugs are therapeutically effective against experimentally induced tuberculosis in guinea pigs (1) has attracted renewed interest in the possibility that a drug may be developed for clinical application in tuberculosis. Some preliminary reports have been encouraging, but they are not conclusive, and several have drawn attention to the unusual difficulties attending investigation in tuberculosis (2 to 9). Investigators have expressed grave concern lest premature or ill-founded conclusions be drawn with resultant wide-spread disillusionment to patients and physicians. Morale is of such critical importance in sanatorium regimen that serious harm may result if patients are misinformed, especially if such misinformation should discourage their acceptance of conventional treatment known to be effective. The following suggestions are offered to investigators who wish to undertake work of this type in the hope that they may be of assistance. They also are for the medical profession as a whole to aid in the evaluation of subsequent clinical reports.

It should be emphasized that the somewhat incomplete studies which have been carried out on the clinical chemotherapy of tuberculosis with sulfone drugs have served a useful purpose (2, 3, 4, 5, 7, 8, 10). These have demonstrated that certain drugs may be administered under careful observation for periods in excess of two years and have indicated the nature of certain undesirable and dangerous side reactions (2, 3, 7, 8, 10, 11, 12). In some of these studies the therapeutic effect demonstrated has been sufficient to indicate the desirability of further investigation, but future studies in order to be valuable must be of an entirely different character with adequate control of the many variables encountered in tuberculosis. It is our belief at this time that little additional information of clinical value is likely to result from extensive repetition of such uncontrolled studies, unless drugs are developed which have a therapeutic efficacy much more obvious than that which has been demonstrated for those drugs (promin, diasone and so forth) which have been studied to date.

The principles of objective experimentation with animals have been clearly established and widely adhered to and the inclusion of an accurately balanced and adequately large group of controls has become a *sine qua non* for any therapeutic experiment. It is our belief that similar exacting standards must be demanded of future clinical studies of this type.

[1] Presented before the Medical Section at the 40th annual meeting of the National Tuberculosis Association, Chicago, Illinois, May 10, 1944.

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EXPERIMENTAL BACKGROUND

Any drug proposed for clinical study in tuberculosis first should have demonstrated several properties:

1: It should have the ability to restrain, arrest or overcome well established tuberculosis in experimental animals, as determined by comparison of survival time and gross and microscopical alteration of lesions with those of adequate controls. The disease should have been permitted to spread and develop in the test animals before institution of treatment. If the drug must be given early in the course of the experimental disease to be effective and is only capable of preventing spread of tuberculosis, it is doubtful if clinical application is justifiable.

2: Experimental animals should be able to tolerate continued administration of the drug in effective doses over periods of many months without critical or irreversible derangement of function or structure of the haematopoietic system, kidneys, liver and so forth. The relationship between minimal effective dose and maximal tolerated dose should be such as to yield an adequate margin of safety to the animals concerned.

3: Adequate test doses should have been administered to human beings prior to institution of any extensive program. The necessary pharmacological data should indicate: (*1*) that the hazards of treatment are absent or are sufficiently slight when compared with the anticipated therapeutic result to justify any discomfort or risk entailed; (*2*) that the nature and potentialities of any undesirable side reactions are known and methods of prevention or early detection of such reactions are available and (*3*) that the drug when given to human beings is absorbed as shown by appreciable concentration in the blood and that the metabolism and method of excretion of the drug are understood adequately whenever possible.

CLINICAL APPLICATION

Selection of patients for clinical study: The success or failure of therapeutic research may depend on the selection of cases for treatment and for a fully adequate control series. Tuberculosis is so notoriously protean in its clinical manifestations and so erratic and unpredictable in its clinical course that critical analysis and classification of clinical material should be applied before cases are selected for study. The apparent pathological nature of the lesions, the extent of the lesions and other factors which might influence prognosis must be considered. As homogeneous a group of cases as possible is desirable.

The belief has been expressed, (2, 3) that exudative pulmonary tuberculosis of recent origin appears to be suitable for chemotherapy because such lesions resemble those successfully treated in animals and because the pathological processes may still be in a reversible stage of development. For this reason, study of this type of lesion is recommended first. After caseation, cavitation and fibrosis have made their appearance, resolution should be slower, less complete and more often dependent on mechanical factors rather than on direct antibacterial action, such as might result from chemotherapy. However, it seems probable that the effect of chemotherapy on each of the many types of

pulmonary and extrapulmonary tuberculosis must eventually be studied. Less confusion will result, however, if investigators will regard these as separate diseases. For example, although the aetiological agent is identical in tuberculous lymphadenitis, in tuberculous meningitis and in the many varieties of pulmonary tuberculosis, the clinical courses are so divergent that the response of each to any effective chemotherapy which may become available should be different.

Classification of cases of pulmonary tuberculosis presents unusual difficulties. Although we must recognize certain deficiencies of the roentgenographic method of diagnosis, this, nevertheless, appears to be the most dependable guide available at this time. Roentgenographic study frequently will reveal fresh exudative disease in association with older lesions of destructive and fibrotic type, the latter being the apparent source from which the recent lesions were derived by bronchogenic dissemination. These recent extensions could constitute suitable lesions for study of chemotherapy if they have not yet advanced to extensive degrees of caseation. Such lesions would appear to be the most frequently available exudative types of disease in the usual sanatorium population and would indicate a lack of effective resistance on the part of the patients. However, since spontaneous remissions of lesions of this type are frequently observed, improvement must not be attributed to chemotherapy unless it is compared with that of an adequate number of similar patients (controls) who did not receive treatment with the drug under consideration.

The numerous factors which affect the prognosis of pulmonary tuberculosis should be considered and should be as carefully balanced as possible in the group of the patients who are to receive treatment with the drug and in the group of those who will not receive the drug (controls). These factors are numerous but include age, sex, race, associated disease (such as diabetes), coöperation and so forth. For example, it might appear that for various reasons patients of adolescent age might prove to be suitable subjects for study. Lesions of patients of this age are unstable and tend either to resolve or to progress rapidly. This makes a large and accurate control group even more imperative than when patients of other age groups are studied.

Bacteriological proof of tuberculosis should be obtained in every case selected for treatment with the drug or as a control, regardless of how typical the roentgenographic picture may appear. It is our belief that bacteriological study of gastric contents, including culture and inoculation of guinea pigs is an indispensable aid. In our studies (3, 8) we have not reported sputum as negative except after repeated negative cultural examinations of gastric contents.

The number of patients selected will depend on the size of the sanatorium and the number of patients willing to volunteer for such treatment. The number of patients required for critical judgment of efficacy of chemotherapy is much greater in tuberculosis than in some disease which has a more predictable clinical pattern. The number of patients required also depends on the type of cases selected. If our suggestions are followed and the lesions selected are of similar character and extent, fewer cases would be required than if many stages and types of tuberculosis were being studied simultaneously.

Some preliminary impressions might be gained from study of smaller groups of patients, such as we and other authors have reported, but significant and unqualified conclusions should be drawn only if the series is large enough to exclude errors due to sampling. It would appear at this time that from 50 to 100 patients should be treated with the drug and a similar number of control patients should be available for an exhaustive investigation. If sufficient uniformity of procedure were followed, it might be possible to pool the results of different investigators, but this adds another factor of uncertainty.

Selection of controls: As stated previously, it cannot be too strongly emphasized that the clinical investigation of the drug should be as well controlled as would be an animal experiment, if equally conclusive results are to be obtained. The truly decisive clinical investigation should be as well founded in facts as a properly executed laboratory study. Although circumstances rarely permit such exactitude in clinical work, it is sometimes necessary to await the performance of such an experiment before an urgent question in clinical medicine can be answered adequately. Such controlled studies were required to prove the efficacy of therapeutic antipneumococcic sera.

The patients available for clinical study should be divided into two groups of equal size with comparable disease and every effort should be made to divide the patients so that all accessory factors which bear on the prognosis should be balanced as accurately as is possible in the two groups. It would be a great advantage if some procedure of chance could be resorted to in deciding which patients are to receive treatment with the drug. In our own studies now under way, pairs of patients who had as nearly comparable disease as possible were selected and the toss of a coin decided which member of each pair was to receive treatment with the drug. The remaining one is considered the control. Administration of inert preparations to the control patients to exclude the factor of mental suggestion also would be of some advantage. No one who has wide knowledge of the pathology and clinical course of pulmonary tuberculosis will have any delusion as to the difficulty in carrying out this important factor of control.

It is possible to compare the clinical progress of a group of patients after treatment with the substance in question to that before the drug was given. It appears highly doubtful, however, whether this method of comparison should be considered as adequate evidence of therapeutic usefulness of the drug if the differences in clinical progress before and after treatment are not of such magnitude or so striking as to exclude the possibility that changes observed are due to the natural evolution of the disease. This method of study has been responsible for many therapeutic errors in the history of medicine.

Administration of the drug: Dose—Although the dosage chosen should not be sufficiently high to produce dangerous toxic reactions, maximal tolerated doses must be administered before a drug may be judged ineffective. At such a high level undesirable side reactions may impinge on the patient's comfort, but uncomfortable reactions should be sharply distinguished from those which indicate actual hazard. Later in the course of the study it would be necessary to reduce dosage adequately in order to ascertain the minimal effective dose.

In so far as possible the dosage should be regulated by objective criteria and determined by the physician, often without the patient's knowledge, especially if the patient is in a position to compare his dose with that of other patients participating in the investigation. As a general rule, however, variable dosage should be discouraged so far as possible in order that the procedure may be repeated more readily by subsequent investigators.

Route and method—The method of administration chosen should be similar to that which has achieved results in experimental animals. It would be preferable not to give the drug parenterally to patients if the oral route has been successful in animal experiments. The compound should be administered at such intervals as may be required to maintain the concentration of the drug in the blood at a constant level, if possible. No drug should be discarded as ineffective if the successful animal experiment has not been adapted as closely as possible to the clinical situation.

Duration of treatment: The observer must constantly keep in mind the pathological nature of tuberculosis and the naturally slow course of the healing process in man. Experience with other forms of treatment, such as collapse therapy, has demonstrated that many months are required for stabilization of an active lesion and pathological studies have shown that potentialities of recurrence are present for years in many instances. Obviously, a rapidly effective bactericidal drug that interrupts the course of tuberculosis promptly would be ideal, but no such drug is on the horizon at present. Drugs which have been studied (promin, diasone and promizole (13, 14)) are not rapid in their action on the disease in experimental animals and it appears that these drugs would not be likely to achieve convincing results unless given continuously for periods of at least a few months. If a time limit must be chosen for drugs which are available at present, we would suggest a minimal period of treatment of two to four months. Tuberculosis cannot be compared to those acute diseases which react so rapidly and favorably to sulfonamide preparations. We have become too accustomed to the miracles wrought by sulfonamide and antibiotic preparations in acute diseases to distinguish lesser or slower effects in their true perspective. Antituberculosis treatment is perhaps more comparable to antisyphilitic treatment.

Selection of institutions: It appears certain that patients subjected to such studies as are described herein should be confined to an institution. Since the numbers of participating patients should be rather large and they should be selected from a still larger group, an institution of considerable size which in normal times would have an adequate professional and nonprofessional staff is usually necessary. The program should preferably be under the supervision of someone who is experienced in problems of research. The clinician should have available for consultation specialists in the various laboratory sciences, especially in the fields of roentgenology and pathology. Laboratory facilities which permit repeated examinations of sputum and gastric contents by most precise methods are basic necessities in such investigations.

Collection of data: If sound decisions are to be made, they must be based on objectively demonstrable facts. Hence it would be necessary to take more frequent and more accurate records of a patient's course if he is participating in

such a program than would be required under routine conditions. Roentgenological examinations and determinations of sedimentation rate should preferably be made once each month and bacteriological examinations of the sputum should be repeated at frequent intervals. All negative microscopical examinations of the sputum, even though concentrated, should be checked by culture or inoculation into guinea pigs (preferably both) and, when the sputum finally is proved negative by these means, similar examinations of several specimens of fasting gastric contents should be made. Haematological examination will be required at least once or twice each week, if patients are being treated with some of the present known drugs (promin or diasone) which have potentialities for affecting adversely the haematopoietic system. Although adequate records of the clinical course should be kept, no dependence should be placed on the patient's testimonial as to his sense of well-being and his personal opinion as to his progress. Only objectively recorded and demonstrable quantitative data should be utilized.

JUDGMENT OF DATA

Under ideal conditions classification and interpretation of results should be entrusted to those who are not directly connected with the patient's care or rechecked by such persons, if this is possible. An impartial and disinterested roentgenologist might be enlisted as a referee whenever possible and the roentgenograms should be interpreted without knowledge as to whether or not patients received treatment. This method is an exceedingly important safeguard because of the subjective factor involved in interpretation of roentgenograms, especially in a field as difficult as that of pulmonary tuberculosis. It is suggested that the roentgenologist should not know about the treatment and perhaps not know the time intervals which have elapsed between successive examinations so that his report will be based entirely on visible phenomena at the time of his review. Subsequently he would want to know much more of the clinical data if he is to assist the clinician in assembling the information in such a manner as to indicate the trend of the disease and the probable pathological processes involved.

It seems important that investigators should report their negative and inconclusive results as well as those which are clearly definitive. Most clinical trials will fall below the standard suggested in this paper. They nevertheless should be reported with a frank admission of all shortcomings appended. Some cumulative information might be gleaned by pooling multiple reports of this character, especially if they indicate similar trends and if they closely adhere to a similar procedure such as that described in this discussion.

COMMENT

This communication must not be interpreted as an indictment of previous incomplete reports, including those which we have published (3, 8). Without exception, such reports have been admitted to be incomplete and of inadequate scope to permit evaluation of the chemotherapeutic compound in question.

These studies and others to follow will serve a useful purpose and the information obtained will be of fundamental value in planning more decisive experiments.

It is extremely difficult to accomplish research under present wartime restrictions. Research in the field of clinical tuberculosis, however, has never been more sorely needed than it is now if the new drugs are to be of any practical benefit in combating the anticipated plague of tuberculosis which is now beginning and which will probably continue in the years that follow the present conflict in Europe. Such research may be truly classified as "war medicine" since tuberculosis may be regarded as a specific pestilence of war along with malaria, typhus and dysentery. When the final summation of the toll of this war is made, it may be revealed that tuberculosis ranks with bombs and bullets in the destruction and crippling of the civilian populations.

SUMMARY

The acceptance or rejection of chemotherapeutic agents, which may be proposed for the treatment of tuberculosis, must depend on experimental and clinical studies which have been rigidly controlled and accurately recorded.

Clinical studies must be preceded by extensive animal experiments; the results should have been confirmed and should indicate clearly a therapeutic effect on established disease of animals.

Preliminary studies should indicate the nature of undesirable side reactions of the drug in the human being and the means of detecting and preventing any dangerous potentialities.

Candidates for clinical study should be selected most carefully and divided into two groups as nearly equal as possible in number of patients, in types of disease, and in other factors which affect prognosis; one group should receive treatment with the drug, the other, which should serve as a control, should not receive treatment with the drug.

The number of patient volunteers participating in such a study must be considerable because of the great variability in the course of this disease.

Emphasis should first be placed on study of those tuberculous lesions of recent origin which are treated before destructive factors have wrought irreversible changes. Type of disease appears to be more important than extent of disease. Bacteriological proof of tuberculosis should be demanded of every case in both groups.

The doses of the chosen drug administered should be as large as can be safely tolerated before the drug is discarded as ineffective. The route of administration should be similar to that which produced successful results in animals. The successful animal experiment should be as closely imitated in all other matters as is possible under clinical conditions.

The response to treatment should be sufficiently prompt and the course of the disease sufficiently unlike that of the control series to make results definite. It is suggested that the data be reviewed by roentgenologists and clinical consultants who have no knowledge as to which patients were treated.

There will likely be urgent need for some more rapid and direct method of treating the large numbers of patients with tuberculosis in the warring nations

of Europe in the near future. All possibilities of chemotherapy for tuberculosis should be explored at this time and these efforts rated as urgent research in war medicine.

REFERENCES

(1) Feldman, W. H., Hinshaw, H. C., and Moses, H. E.: Promin in experimental tuberculosis: Sodium p,p′-diaminodiphenylsulfone-N,N′-didextrose sulfonate. Am. Rev. Tuberc., 1942, *45*, 303.

(2) Zucker, G., Pinner, M., and Hyman, H. T.: Chemotherapy of tuberculosis: Promin by the intravenous drip method, Am. Rev. Tuberc., 1942, *46*, 277.

At this early date it seems evident that the clinical trials have not justified the optimism and enthusiasm which laboratory experiments indicated. Furthermore, it has become evident that, in therapeutic experiments on human beings, great care must be exercised lest the patients build up a false or unwarranted hope of cure. Nothing stimulates hope in a tuberculous individual more than the promise of a new "cure," and nothing is more depressing than the disillusionment of failure.

For these and other reasons, the leaders in tuberculosis in general, and the Trudeau Society in particular, have recognized the wisdom of keeping the work under rigid control until it can be announced without doing harm, and at the same time to lend full coöperation and encouragement to further experimentation. The time has come, therefore, to assess and regulate methods of procedure.

Doctor Hinshaw has admirably outlined the subject and has made an auspicious beginning in reaching the desired objective. With minor exceptions encumbent on any work with tubercle bacilli, the experiments of Doctors Hinshaw and Feldman have been models of perfection. Their work on experimental tuberculosis in animals has also been the most effective therapeutic study on animal tuberculosis to date. Perhaps by oversight or for lack of time, nothing was said about *in vitro* tests which may be used to great advantage in the preliminary screening of unknown drugs. In the administration of drugs, continuous injection also may be desirable.

The authors have quite properly stressed the fact that animal experiments cannot be applied directly to the protean human disease. This important feature of tuberculosis has been disregarded too much in the past and still does not have a full meaning to many clinicians and tuberculosis workers. It should be realized that tuberculosis is the resultant of two interacting biological variables—a host that varies with age, race, sex, etc., and a parasite varying with dosage, virulence, type and certain physical characteristics common to very few other bacterial species. There may result, on the one hand, a benign disease which heals, and, on the other hand, a violent and progressive fatal pneumonia and septicaemia. In between these two extremes exist hundreds of intermediate forms.

Even after selecting controls, patients that match in every way, the location of bacilli with respect to blood vessels, bronchi, vital organs (adrenals, meninges, etc.) are unknown. Neither can the possibilities of spontaneous increase or decrease in virulence be foretold. The only safeguard against such unforeseen variations and accidents resulting from them is to use a large series of controlled cases.

The size of the institution is significant. Because small institutions cannot have adequately matched controls, they are handicapped in a therapeutic program. Larger institutions do not have the same objectionable features, although there may be some faults not inherent in small institutions. Certainly the matching of controls in larger institutions is simpler, although still imperfect.

Perhaps the most difficult feature to control is the patient's psychological attitude.

Physical signs and symptoms are difficult to evaluate as are roentgenological findings.

The method of matching controls is perhaps a subject that most workers will be interested in and one which we have spent much time in developing. Without any pretense at completeness or finality and with full recognition of numerous shortcomings and deficiencies, I should like to explain the methods we have adopted in our Institution.

At the present time we are doing more acceptable work than was done in the first work the writer attempted, twenty years ago, with a certain serum prepared in asses. I believe that small completely negative series were the first matched control therapeutic experiments in human tuberculosis in this country. Then, the work on sanocrysin followed shortly.

The important feature in the sanocrysin studies was the proof of the need for the control in clinical experiments. We were not able at first to control the treated patients because some interested and well meaning lay people insisted that nobody be denied the cure which the newspapers had hailed so widely. Several controls, however, were belatedly made. Patients who resided in the institution during the same period of time were matched against the treated cases. Another group received injections of salt solution for a period of weeks and then, without notice were switched to gold and the two periods of treatment were compared. Many cases appeared to undergo rapid improvement—certainly there was a rapid temporary change—but the controls were inadequate and matched controls were finally adopted and used in a large series of cases, and have been used in every therapeutic experiment since. Coincidentally, Amberson, McMahon and Pinner (5) used matched controls in their experiments on sanocrysin and reported negative therapeutic results. The fact that gold has practically disappeared from use speaks well for their methods of control as well as for their results and conclusions.

In 1941, the writer, with Dr. A. J. Carlson and associates (6) of the Department of Physiology of the University of Chicago, worked on a large therapeutic experiment in tuberculosis with vitamin C. In this instance there were no restrictions on control work and here again the matched controls spoke more eloquently than any words and proved that beneficial results in animals cannot be applied directly to human beings. The results of the experiment were clear-cut and final. Aside from the benefits of supplying depleted vitamin C and correcting the effects of its deficiency, there was no virtue in vitamin C against the tubercle bacillus and tuberculosis. This work established the value of matched controls beyond any doubt.

In human experiments we fully agree that the minimum plan should include from 50 to 100 patients, but the original selection must be much larger. In the vitamin C experiments referred to, 428 patients were needed in all to obtain about 120 suitable cases for treatment, only about half of whom remained to the end of the experiment. The casualty among patients is great if the experiment lasts over a year and if sufficiently ill patients are selected; many also leave for one cause or another.

The extent of disease is another feature that must be given consideration. Obviously, most mi nimal and many moderately advanced lesions will recover without anything but bed-res t—some without even that. On the other hand, lesions too far advanced will die too soon and will not be a fair criterion.

Early far advanced cases with stabilized disease, therefore, seem to be the best suited for clinical experiments.

The quality of disease is also important. It is obviously not fair to compare a patient having a disease process of a few months with one of many years, or a caseous pneumonia with fibroid disease. All severe complications should be ruled out, as well as all cases receiving any other therapy, including collapse therapy. Exceptions may be made of early

enteritis or laryngitis, providing they are matched with others having complications similar in quality and quantity. Complications of other diseases are not acceptable, such as syphilis, nephritis, heart disease, peptic ulcer, amyloidosis, diabetes, effusions, etc.

After a preliminary selection of acceptable cases, the second stage of selection is carried out by more careful clinical, X-ray and laboratory studies. Blood chemical examinations, including sedimentation rate, plasma proteins and nonprotein nitrogen; blood cytology; urine and sputum examinations are performed. When all data are assembled on specially prepared cards, each deviation from normal is given a negative numerical value or "handicap" in proportion to the particular factor deviating from the normal.

After all factors are evaluated and totalled, the result is called the "prognosis quotient," which usually ranges from 200 to 500. In matched cases the prognosis quotient of each pair has been kept within 50 points, usually within 10 to 15 points. All the cards bearing the full data are laid in two piles—one to be treated and the other to be used as a control. By a flip of a coin, the higher name in the alphabet of each pair is treated or used as control, as the case may be.

During treatment all pairs of patients must be treated in the same manner, as far as possible, except one is to receive the drug while the other is to get a disguised placebo. The experiment should be carried out so that everybody concerned knows only one phase of the work. In that way each is a check upon the other, and the result will be free of any bias by suggestion.

Close observation is necessary, especially with the sulfa drugs, because destruction of red blood cells occurs in some cases. Repeated blood counts must be made to forestall any unfavorable reaction. Chemical analysis should be done on blood and urine to see whether the patients are taking the drug and also to see whether any retention of the drug is present. Chemical and microscopical urine examinations are also essential. Many patients complain of weakness, others nausea, others headaches, all of which must be watched closely.

An evaluation of all factors is made at three- and six-month intervals and compared with the figures obtained at the beginning. At the end of three or six months the "prognosis quotient" in the treated cases should be much less than the controls if the remedy is effective.

All details cannot be given in this brief discussion, but enough has been presented to demonstrate a workable method that has served in the past and one that, with modifications, may develop into a better plan for the future. To this end, we solicit aid from our colleagues and offer a hearty coöperation in the effort.

REFERENCES

(1) Feldman, W. H., Hinshaw, H. C., and Moses, H. E.: Effect of promin (sodium salt of p,p′-diaminodiphenyl-sulfone-N,N-dextrose sulfonate) on experimental tuberculosis: A preliminary report, Proc. Staff Meet., Mayo Clin., 1940, *15*, 695.

(2) Karasch, Morris, and Reinmuth, Otto: Chem. Abstracts, April 20, 1943, *37*, 2140. U. S. Pat. No. 2,300,677 to Ely Lily & Co.

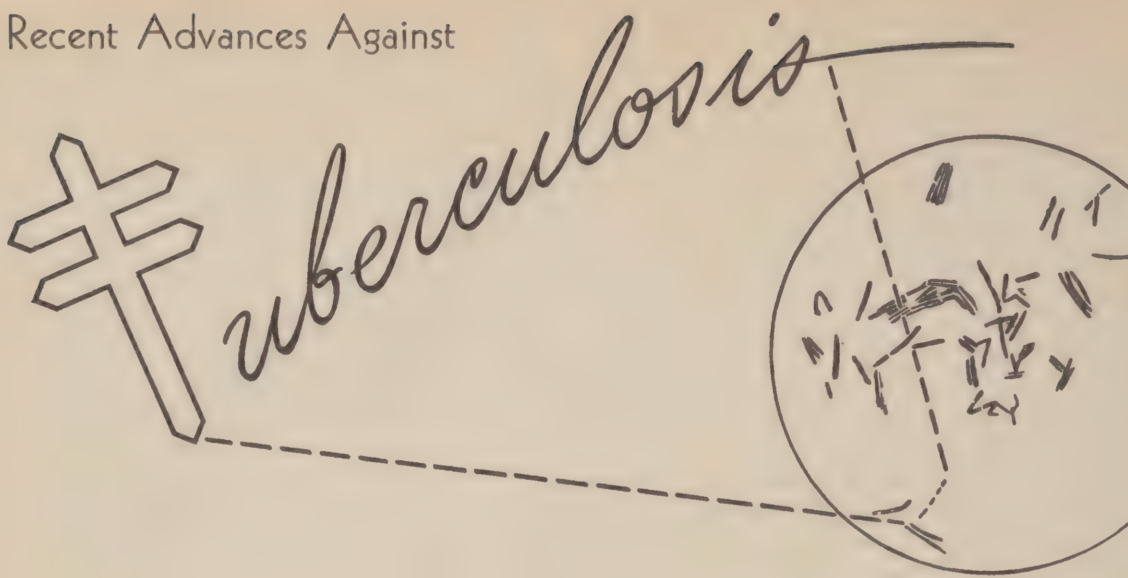
(3) In preparation for publication.

(4) Petter, C. K., and Prenzlau, W. F.: Treatment of tuberculosis with diasone, Am. Rev. Tuberc., 1944, *49*, 308.

(5) Amberson, J. B., Jr., McMahon, B. T., and Pinner, Max: A clinical trial of sanocrysin in pulmonary tuberculosis, Am. Rev. Tuberc., 1931, *24*, 401.

(6) Sweany, H. C., Clancy, C. L., Radford, M. H., and Hunter, V.: The body economy of vitamin C in health and disease, J. A. M. A., 1941, *116*, 469.

Recent Advances Against Tuberculosis



SULFONE DRUGS MAY OPEN A NEW APPROACH TO CONTROL OF THE DISEASE WITH HIGHEST MORTALITY AMONG AMERICANS BETWEEN 15–45

SINCE Pearl Harbor more Americans have been killed by tuberculosis than by enemy bombs and bullets. Each Yuletide season the Christmas seal campaign underscores the continuing need for united action by public health agencies to control and conquer the ravages of the tubercle bacillus.

This year there is new hope that drug therapy may at last provide an effective treatment. Interest has centered on three derivatives of diaminodiphenylsulfone: diasone (disodium formaldehyde sulfoxylate diaminodiphenylsulfone), promin (sodium *p,p′*-diaminodiphenylsulfone N,N′-didextrose sulfonate) and promizole (4,2′-diaminophenyl-5′-thiazolesulfone).

Despite glowing reports in the lay press and some other publications, none of the three has been proved sufficiently effective and safe for general distribution. None has been subjected to controlled clinical study. While there are indications that all three drugs may have some value as an adjunct to other methods of treatment, the therapeutic effect is not sufficiently striking to make it certain, in the absence of adequate controls, just what influence the drugs have had in reported cases of clinical improvement.

To avoid false hopes and disappointment, pharmacists should tell inquiring physicians and patrons that all of the sulfones are still experimental therapeutic agents and will not be available in the near future. Meanwhile, experiments are continuing in a number of clinics and laboratories.

Studies on diasone are probably most advanced. Raiziss and his co-workers, who reported on the synthesis and chemical properties of the drug in the Scientific Edition of THIS JOURNAL, point out that diasone first received attention because of its effectiveness against streptococcic and pneumococcic infections of mice.

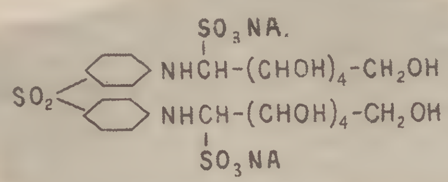
Later other workers found that diasone favorably altered the course of experimental tuberculosis in guinea pigs. Few clinical data have been reported in the medical literature although investigations have been under way in several sanatoriums. Both the National Tuberculosis Association and the American Trudeau Society have committees which are now trying to evaluate this chemotherapeutic agent.

Tests on experimental tuberculosis in guinea pigs led Callomon and Groskin to conclude that diasone is preferable to the related drug, promin, mainly because of lower toxicity.

After tests on animals had shown that promin inhibited the development of tuberculosis much like diasone, limited clinical trials were under-

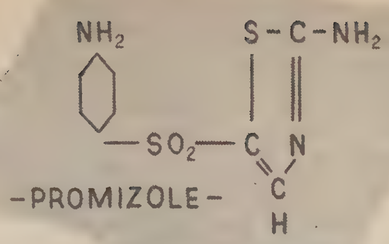
taken, particularly at the Mineral Springs Sanatorium, Cannon Falls, Minnesota, in cooperation with the Mayo Clinic. Experiments have shown, according to Hinshaw, Pfuetze and Feldman, that prolonged administration of promin orally is clinically feasible and that the results obtained justify further work. Observation of a small series of cases since 1941 indicates that the reversal of unfavorable clinical trends following administration of promin for four to twelve months, which was previously reported, has continued. The Mayo workers, however, "found it difficult to state with absolute conviction that chemotherapy was the crucial factor in the recovery of any of these patients from tuberculosis."

At the National Leprosarium in Louisiana, physicians of the U. S. Public Health Service who have tried promin consider it the most encouraging experimental treatment for leprosy they have used. The tests were suggested by the fact that the bacteria which cause tuberculosis and leprosy are closely related morphologically. Commenting on the use of promin, the physicians state that they "consider it an advance in the right direction in the chemotherapy of leprosy and hope that further synthesis of the sulfa chemicals will produce a product which has specific properties against *M. leprae* and *M. tuberculosis.*"



-PROMIN-

A further step toward this goal came with the synthesis of promizole in 1942 and its subsequent trial on both experimental tuberculosis in guinea pigs and clinical cases. Workers at the Mayo Foundation report that promizole is comparable to diasone and promin in its ability to convert progressively destructive disease in guinea pigs



-PROMIZOLE-

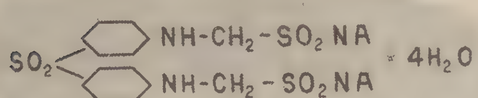
to an arrested or nonprogressive stage in which morbid changes may be resolved. It apparently has the great advantage of being much less toxic than other drugs that have shown some action against tuberculosis.

That promizole has little, if any of the hemotoxic properties that have so limited the clinical application of other sulfones seems to be demonstrated by a preliminary report on the treatment of 56 patients by Hinshaw and co-workers. Because of the lack of adequate controls and the small number of patients treated with promizole to date, clinical results cannot yet be evaluated satisfactorily.

Hinshaw says: "Present incomplete evidence indicates that promizole is at least as effective as any previously described compound in the treatment of experimental tuberculosis of guinea pigs but is unique among the numerous compounds which we have studied in being easily administered, well absorbed and of extremely low toxicity for human beings.

"Clinical studies in chemotherapy of tuberculosis and of leprosy have been sufficiently encouraging to arouse hopes that chemotherapy of mycobacterial diseases eventually might attain a practical stage of development."

An interesting sidelight on current research is the unexpected "immunity" which develops in infected guinea pigs after chemotherapy. At least two different research teams have reported experiments which show that guinea pigs may live many months after discontinuance of successful chemotherapy, even though fully virulent bacilli can be found in their organs. This is of



-DIASONE-

particular interest because guinea pigs, unlike man, possess so little natural resistance to tuberculosis that an infection usually runs a rapid and fatal course. Recent experiments, some as yet unpublished, indicate that the "immunity" may be gradually lost after a period of months. No similar increase in resistance following chemotherapy has been observed in human beings, and because natural resistance to tuberculosis in man is extremely difficult to measure, it would be very difficult to demonstrate.

Search for Effective Drug

Efforts to find an effective drug for the treatment of tuberculosis have been in progress for centuries. The search for a chemotherapeutic agent appears to have been originally stimulated by Ehrlich's researches on arsenicals for the treatment of syphilis.

Since that time pharmacists and physicians have studied gold, copper and calcium salts, guiacol, sulfonamides and other compounds. Although some have been sporadically and hopefully tried clinically, none has received general acceptance as having any specific effect.

Many pharmacists will have noted that the standard prescriptions for the tuberculous are usually a cough sedative, such as codeine sulfate, and an expectorant, such as ammonium chloride.

There is no doubt that thousands of undiagnosed cases advance beyond hope of cure due to self-medication with sedatives and expectorants for a "cold that hangs on" or "chronic bronchitis." Pharmacists should keep this in mind when patrons request over-the-counter dispensing for such conditions. Expectorants containing iodides even produce irritative reactions of tuberculous lesions and may activate an otherwise dormant case.

Contrary to popular belief, the characteristic symptoms of hemorrhage, marked loss of weight, lack of appetite, etc., do not show up in a large percentage of cases until the disease is far advanced. Furthermore, tuberculosis often assumes the guise of relatively harmless infections of the upper respiratory tract. Prompt medical diagnosis often means the difference between speedy recovery and years of invalidism or death.

This is emphasized by the fact that at present, and at least in the immediate future, physicians must rely primarily on aiding the patient's natural defense mechanism to overcome the disease. In pulmonary tuberculosis, by far the most prevalent type, this means some form of rest. Few chest specialists any longer believe that change of climate or fresh air "cures" are an important factor in recovery, except in selected cases.

While rest in bed is usually an indispensable part of the regimen, surgery has devised ways of holding the diseased lung almost completely at rest. When both lungs are infected both can be held partially at rest. A sedentary patient can get along on the oxygen supplied by only a fraction of his lung capacity. Modern refinements in this technique are saving thousands of lives each year.

The objective of all surgical methods of this type is collapse of the lung. The first such procedure to be developed, and now most widely used, is called pneumothorax. Air is introduced between the chest wall and the lung through a small needle, which overcomes the natural vacuum in the chest cavity. This restricts the movement of the diseased lung, and the degree of collapse or rest can be adjusted by varying the amount of air introduced. Periodic refills are made as the air is gradually absorbed.

A second procedure is to remove sections of ribs, called thoracoplasty, which reduces the area of the chest cavity and partially collapses the lung. The disadvantage of the operation is that results are permanent, while pneumothorax can be discontinued when the lung has healed. This, plus the seriousness of the operation, has largely limited its use to those cases in which other measures are inadequate or cannot be used.

Crushing Nerves

Lung collapse can also be achieved by cutting or, more commonly, crushing the phrenic nerve. The two branches of this nerve run from the brain down each side of the neck and terminate in the diaphragm. By surgically crushing the nerve on the side of the infected lung, that side of the diaphragm is temporarily paralyzed. The immobile arched diaphragm thus restricts the movements of the lung, greatly increasing the body's chance of overcoming the disease process.

During the past twenty years more and more surgeons have become trained in these successful techniques. This, together with increased clinical and public health facilities through various agencies, has resulted in reducing the death rate from tuberculosis by three-fourths since the turn of the century. Yet, the limited funds of patients

and of local health departments and inadequate case finding programs have permitted tuberculosis to remain in first place among fatal diseases of Americans in the age group between 15 and 45.

Therefore a new national attack on the problem will soon get under way through the Tuberculosis Control Division just established in the U. S. Public Health Service. Surgeon General Thomas Parran has picked a young Minnesotan, Dr. Herman E. Hilleboe, to head the campaign.

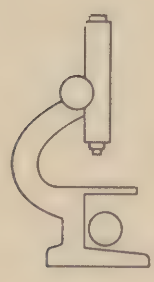
Representatives of the Public Health Service have been out consulting with the states to see how much money and what facilities will be needed. Dr. Hilleboe and his associates are now going over the data and sometime in December expect to present to Congress their war budget against tuberculosis. An appropriation up to $10,000,000 for 1945 was authorized in July.

No federally controlled and Washington administered program is contemplated in the usual sense. Instead about 85% of the funds will be distributed as grants-in-aid to states on request, with allotments based on population, extent of the problem and financial need. Part of the funds will be matched by state appropriations.

Medical and nursing staffs will be increased, laboratories improved and clinical and x-ray facilities installed under plans developed by each state. Local mobile x-ray units, using the new economical miniature films, will tour the country-side, hunting for unsuspected cases which may be spreading the infection to family and friends.

About a tenth of the funds will be used by the U. S. Public Health Service itself for a public and professional demonstration program to try to make the knowledge and use of tuberculosis control methods available to every community in the country.

About 5% of the funds for the new program is expected to go into research on promising new drugs and other new methods of control and, through cooperation of other research groups, to correlate work already done. If, as now seems likely, an effective chemotherapeutic agent for tuberculosis is developed, it will at one stroke greatly reduce the annual toll of the disease in lives and money. In this, pharmacy—through research, manufacturing laboratories, and retail and hospital pharmacies—will play an important role.



BCG VACCINE[1,2]

Its Preparation and the Local Reaction to Its Injection

JOSEPH D. ARONSON, ERMA I. PARR AND ROBERT M. SAYLOR

The protective value of BCG vaccine against tuberculosis in man has not been definitely established and the results claimed for this vaccine lack uniformity. This may be due, in part, to variations in the technique used in maintaining stock cultures and to differences in the age and rate of growth of the culture, as well as to variations in the number of viable organisms and the dose and route of administration of the vaccine. The demonstration of allergy, following vaccination, is also dependent upon variable factors such as the dose and route of administration of the vaccine, the time elapsing after vaccination, the dose and potency of the tuberculin and the technique employed in tuberculin testing. It is difficult to estimate the rôle that BCG vaccination plays in protecting man against infection with the tubercle bacillus because of the impossibility of determining definitely the degree of reinfection with tubercle bacilli of varying virulence, and because of the difficulty of estimating the natural resistance of the individual.

In order to obtain more precise information on the preparation and protective value of BCG vaccine, the present study was carried out under controlled conditions on a population in its natural habitat, without modifying the mode of living or degree of exposure to tuberculosis.

From February, 1936 to February, 1938, 1,565 persons ranging in age from one to nineteen years were vaccinated intracutaneously with BCG vaccine. During the same time, 1,460 persons of the same age and sex, living in the same area and under the same conditions, were injected with 0.1 cc. of sterile physiological salt solution and served as controls. Before their inclusion in this study both the vaccinated and control groups had failed to react to the injection into the skin of 0.000,02 and 0.005 mg. of PPD. With few exceptions the chests of the members of the two

[1] From the Office of Indian Affairs, Department of the Interior, Washington, D. C., and The Henry Phipps Institute, University of Pennsylvania, Philadelphia, Pennsylvania.

[2] This investigation was aided by the National Institute of Health of the United States Public Health Service as part of a coöperative study.

groups were X-rayed either before or shortly after they were vaccinated or included as controls. The members of both groups have been retested with the same preparation of PPD and X-rayed at yearly intervals.

This study was conducted on different tribes of American Indians of varying degrees of blood admixture, living on the Gila River Reservation, Arizona, the Wind River Reservation, Wyoming, the Turtle Mountain Reservation, North Dakota, the Rosebud Reservation, South Dakota and on nonreservation Indians of southeastern Alaska. These Indians, living under widely different climatic conditions, are for the most part indigenous to their present locality. While they vary widely in their physical characteristics, dietary habits and social and economic patterns, their economic level is almost uniformly low.

CULTURAL AND BIOLOGICAL CHARACTERISTICS OF BCG

Of the 1,565 children vaccinated intracutaneously with BCG, 1,053 were injected with a vaccine prepared from strain number 317, while 512 received a vaccine made from strain 575. Strain 317 was received at the Henry Phipps Institute, Philadelphia, March, 1928 from Dr. M. J. King, Hegeman Laboratory, Metropolitan Life Insurance Company, Mt. McGregor, New York. This culture was obtained by Doctor King from the late Dr. W. H. Park, New York City Board of Health Laboratory, and was a transplant from the culture received by Doctor Park in 1926 from Prof. A. Calmette, Pasteur Institute, Paris. Strain 575 was received by one of us in January, 1938 from Prof. M. Guérin, Pasteur Institute, Paris. Strain 317 has been kept under lock on a floor of the Phipps Institute which is not used for any other studies in bacteriology or pathology. No other strain of tubercle bacillus or cultures of other bacteria have at any time been kept in the same room or incubator. Equipment and supplies used at the Henry Phipps Institute for studies on the BCG vaccine were new and their use was strictly limited to the maintenance of the BCG culture and the preparation of the vaccine. The stock strains were grown on potato soaked in veal infusion broth, and were subcultured upon this medium, at intervals of two weeks. After 10 transplantations the cultures were grown for 3 generations on potato soaked in beef-bile, containing 5 per cent glycerine broth, when they were again transplanted to the bile-free potato medium.

The colonial characteristics of strain 317 have been observed by one of us (JDA) since 1928. On potato soaked in glycerol-veal-broth, colonies visible to the naked eye appeared in from seven to ten days after inoculation. These colonies, at first cream colored, later changed to pale yellow and covered the surface of the medium. They appeared as elevated, dry, crumbly and irregular masses. Magnified ten times the larger colonies were found to consist of 8

to 10 small rounded confluent colonies of waxy appearance, forming a morula-like mass. The centre of these colonies was translucent with a moth-eaten appearance, while the periphery was opaque and thickened. Upon potato media soaked in beef-bile containing 5 per cent glycerine the culture was slightly elevated and grayish, with a smooth, dull surface. Along the free borders large rounded colonies resembling drops of wax were present. On Sauton's medium with a pH of 7.2 to 7.3 a thin, pale yellow, wrinkled film, covering about one-third to one-half of the surface, was noted seven to ten days after inoculation. At the end of the second week this film, in most instances, had spread over the surface and extended for a short distance along the sides of the flask. It was frequently observed that after the sixth or eighth generation on Sauton's medium the BCG culture grew poorly. The colonies were fused, and the film, which had a mesh-like, dry appearance, sank readily when wet by the culture medium. In addition to these types of growth there were also observed, from time to time, slowly growing, small, dry, grayish, rounded colonies with hollow centres resembling doughnuts. When transplanted to Sauton's medium these colonies either failed to grow or grew very slowly. At times the three types of growth occurred in the same flask, but more frequently only two types were present.

The BCG strain 575, which was received January, 1938 from Prof. Guérin, Pasteur Institute, Paris, presented the same cultural characteristics on potato as did strain 317. On Sauton's medium this strain dissociated into discrete rounded, waxy colonies which sank readily when touched, and flat, dry, mesh-like white or pale yellow colonies with irregular edges, which rapidly covered the surface of the medium.

The avirulence of these strains of BCG was determined, at intervals, by injecting 30 mg. of each culture into the peritoneal cavity of normal guinea pigs. These animals were kept under observation for three to four months, when they were killed and necropsied. Up to the present time neither one of these two cultures has produced any evidence of generalized tuberculosis in any of the inoculated animals.

We have had no proof of any increase in the virulence of the BCG culture. The possibility that prolonged cultivation on artificial media may lead to a loss or modification of the antigenic properties of the culture cannot be denied. To estimate the efficacy of the vaccine we have determined, from time to time, its protective value on animals. Normal guinea pigs injected subcutaneously with 5 mg. of BCG vaccine were reinfected six weeks later, either intratracheally with approximately 100 virulent bovine type tubercle bacilli, or subcutaneously with either 0.01 or 0.001 mg. of a virulent human type culture of tubercle bacillus. Concurrently an equal number of unvaccinated guinea pigs were infected

by the same route and with the same amount of culture. The vaccinated as well as the unvaccinated control animals were killed and necropsied six weeks later. Aronson (1) found that BCG-vaccinated guinea pigs reinfected intratracheally with virulent tubercle bacilli show fibrous or fibrocaseous hilar lymph nodes, as well as a small number of fibrous or fibrocaseous tubercles in the internal organs, but no microscopically demonstrable tubercle bacilli. On the other hand, among the unvaccinated control animals the hilar nodes were caseous, extensive tuberculosis with softening was observed in the internal organs and lymph nodes, and microscopical examination revealed numerous tubercle bacilli. When the vaccinated guinea pigs were injected subcutaneously with virulent tubercle bacilli, scant tuberculosis of the internal organs was observed and the regional lymph nodes had thin milky fluid in the centre. Among the control animals, similarly infected, extensive tuberculosis of the internal organs and lymph nodes was observed and the regional lymph nodes were caseous.

PREPARATION OF BCG VACCINE

In order to control the preparation of the BCG vaccine and to have available a uniformly fresh supply, vaccine was prepared as needed at each reservation. A mobile laboratory, containing the necessary equipment, chemicals, incubator and other supplies, was organized and was transported from place to place by car. To avoid all possibility of contamination with virulent tubercle bacilli it was considered advisable to establish the laboratory in a school house rather than in the local hospital. No sputum or other material suspected of being contaminated with tubercle bacilli or other bacteria was permitted in the laboratory, and no other strain of tubercle bacillus or cultures of any other bacteria were kept in our possession. All supplies and equipment used in the course of this investigation were new and their use was strictly limited to the cultivation and preparation of the BCG vaccine.

The stock BCG strain was cultured as previously described. For preparing the vaccine the culture was transplanted from the bile-free potato medium to the surface of Sauton's synthetic medium, where it was grown for varying periods of time.

Of the 13 preparations of vaccine used in this study, 7 were made from strain 317 and 3 from strain 575, all grown on Sauton's medium, while 3 preparations were made from strain 317 grown on potato soaked in veal-infusion broth. Vaccine was prepared from cultures grown at

38°C. for from seven to thirty days. The bacillary growth was collected from the surface of the culture medium by means of a heavy platinum wire and the excess fluid was removed by placing the bacillary mass between several layers of sterile filter paper. The bacillary mass was weighed on a sterile platinum foil, and was ground in a sterile agate mortar until it formed a thin uniform paste. Sufficient sterile physiological salt solution was added, gradually, to make the desired concentration. More recently we have prepared the vaccine by grinding the bacillary mass in a sterile round-bottom glass flask containing stainless steel balls approximately 4 mm. in diameter (2), and gradually adding the required amount of sterile salt solution. This simple modification has facilitated the preparation of the vaccine and minimized the danger of contamination.

The absence of contaminating organisms in the vaccine was determined by inoculating 2 cc. of the vaccine into Dunham tubes containing one per cent dextrose broth. The BCG vaccine was then distributed in vials packed in a vacuum jar containing ice, and used within three days, although most of the injections were made within the first twelve hours. In Alaska it was found more practical to prepare the vaccine at Juneau and fly to the different villages so that the vaccinations could be completed within three days.

TECHNIQUE OF VACCINATION

With few exceptions, vaccination with BCG vaccine was made in from two to three weeks after the person failed to react to the intracutaneous injection of 0.000,02 and 0.005 mg. PPD. In a small number of cases a period of from four to five weeks elapsed between the tuberculin testing and vaccination.

The preliminary procedure used for the administration of the vaccine consisted of painting the skin over the region of the right deltoid muscle with tincture of iodine, followed three to five minutes later by washing this area with 95 per cent ethyl alcohol. When the skin had dried, 0.1 cc. of the vaccine, containing either 0.1 or 0.15 mg. of the BCG culture, was injected slowly into the dermis by means of a sterile tuberculin syringe and a 26-gauge platinum needle. An attempt was made to make these injections as uniform as possible, but differences in the texture of the skin, as well as variations in the depth of injection, may have contributed to the variations in size and appearance of the resulting nodule.

The site of the injection was examined forty-eight hours later for

evidence of a Koch phenomenon as a further check on the tuberculin-negative state of the subject, and subsequent examinations were made at weekly intervals until the ulcer had healed. Of the 1,565 persons injected with the BCG vaccine, the Koch phenomenon was observed in only 5 instances. In 3 of these the injection of BCG vaccine was made because of mistaken identity, in tuberculin-positive cases. In the remaining 2 cases a period of five weeks had elapsed between the time of tuberculin testing and vaccination. One of these 2 cases died from miliary tuberculosis two months after vaccination, while the other case is alive. In both instances there is the possibility that the negative tuberculin reaction occurred during the preallergic period or that infection with virulent tubercle bacilli happened subsequent to the tuberculin test. In no instance did the introduction of the BCG vaccine in tuberculin-positive or in any of the tuberculin-negative cases elicit any untoward local or general reactions.

REACTION FOLLOWING BCG VACCINATION

The character and intensity of the local inflammatory reaction induced by the intracutaneous injection of BCG vaccine was not modified by sex, degree of Indian blood or constitutional type. It was noted, however, that the reaction was less marked among the younger children of preschool age, and that, in general, the ulcers healed more promptly among those living in Arizona than among those in Alaska.

In general, comparable types of inflammatory reaction and ulceration were induced by vaccine lots 1 to 7 inclusive, and 11 to 13 inclusive, while less marked inflammatory reaction was noted following the injection of the same amount of vaccine from lots 8 and 9.

The intracutaneous injection of either 0.1 or 0.15 mg. BCG vaccine was followed forty-eight hours later by the appearance of a sharply defined nodule measuring about 4 mm. in diameter and 1 mm. in height. During the first two weeks after vaccination the local inflammatory reaction became less marked, while the nodule gradually increased in size to an average of 6 mm. Three to four weeks after vaccination there was observed a rapid increase in the size of the nodule, and in many instances a definite central area of softening was palpable. Ulceration occurred by the fourth week in approximately 75 per cent of cases and persisted for from four to eight weeks. A sense of fulness in the axilla of the vaccinated side and a dull aching pain at the site of injection were the subjective symptoms noted in a large number of cases. With

the onset of ulceration and the establishment of drainage, pain at the site of injection and the sense of fulness in the axilla disappeared. In about 5 per cent of the cases enlargement of the regional lymph nodes along the anterior axillary fold was noted. In no instance did the lymph nodes ulcerate, nor did the local ulcer ever require surgical intervention. In the vast majority of cases healing was completed approximately twelve weeks after the injection of the BCG vaccine, leaving a depressed soft scar measuring from 5 to 10 mm. in diameter.

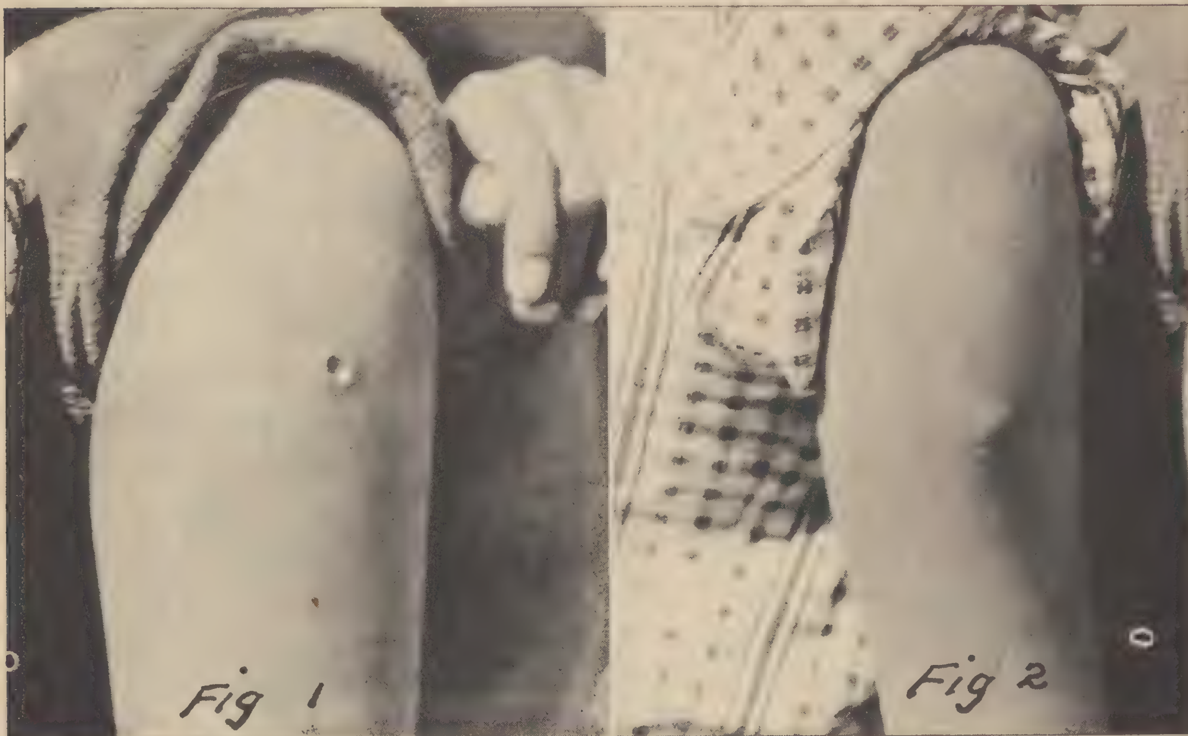


FIG. 1. Ulcerative lesion six weeks after intracutaneous injection of 0.15 mg. BCG (preparation number 2, page 653). For detailed description see page 658.

FIG. 2. Soft nodular lesion six weeks after intracutaneous injection of 0.15 mg. BCG (preparation number 2, page 653). A minute ulcer is present, not visible in the photograph. For detailed description see page 658.

We have observed, under comparable conditions of dose, preparation of vaccine, climate, tribe and degree of Indian blood, that definite variations in the intensity and character of the local reaction follow the injection of BCG vaccine. These variations may be due in part to differences in individual resistance or to a lack of uniformity in the administration of the vaccine, although all of the injections were made by one of us, who exercised care in making the injections as uniform as possible. It was noted, forty-eight hours following the injection, that

the character of the local inflammatory reaction differed. In some instances the resulting nodule was sharply defined, deep and, with increasing time, hard and shotty to the touch, while in other instances the inflammatory reaction was diffuse, firm, gradually merged into the surrounding tissue and was at no time sharply defined. With the development of ulceration, additional differences were observed. In approximately 40 per cent of cases the ulcer appeared as a sharply defined, punched out, more or less circular lesion resembling a syphilitic chancre. The walls and base of the ulcer were covered by granulation tissue, the margins were not undermined and the ulcer tended to heal promptly (figure 1). In the remaining 60 per cent of cases there was softening in the centre of the diffuse nodule, followed by the appearance of an ulcer approximately 1 mm. in diameter, from which, on pressure, there escaped thick, grayish white and, at times, blood-streaked pus. The ulcer gradually enlarged and the lesion resembled the typical tuberculous ulcer with its undermined edges and small crater-like opening. This type of lesion persisted for a long time, healed more slowly and resulted in larger scars than did the ulcers described previously (figure 2).

Preparations made from the pus of the different lesions, when stained by the Ziehl-Neelsen method, revealed large numbers of polymorphonuclear cells, occasional large mononuclear cells and a few small lymphocytes. Clumps of uniformly staining acid-fast bacilli, some of which were phagocyted by polymorphonuclear cells, were seen. Smears made from these ulcers at weekly intervals showed a decrease in the number of polymorphonuclear cells, and a gradual increase in the mononuclear cells, with a marked increase of fibrin, but no conspicuous increase in the number of small lymphocytes. The number of acid-fast bacilli in the exudate decreased rapidly, and in preparations made six to eight weeks after vaccination the bacilli were found to be faintly staining and granular. Contaminating bacteria were not observed in the exudate in association with the acid-fast bacteria until after the disappearance of the latter organism, when staphylococci and other cocci were observed in a small number of cases.

VARIATIONS IN ANTIGENICITY OF VACCINE

The effects of age of the culture dose and number of generations on bile-free medium on the antigenicity of the BCG vaccine were determined by comparing the percentage of vaccinated children who reacted to tuberculin one year and two years after vaccination with the different preparations of vaccine.

While we have employed the tuberculin reaction as a criterion of the antigenicity of the vaccine, we do not imply that allergy and immunity are necessarily identical.

The effectiveness of BCG vaccine is dependent upon the number of viable organisms present in the vaccine; the number of such organisms decreases with the increasing age of the culture. The age of the cultures used in preparing the vaccine ranged from seven to thirty days. It will be observed from table 1 that the age of the culture, as far as can be determined from this study, influences neither the sensitivity to tuberculin, as indicated by the reaction to the two different doses, nor the total number of positive reactions.

That the attenuation of the original virulent bovine strain of tubercle bacillus resulted from the addition of beef bile to the culture medium is the view expressed by Calmette and Guérin (3). However, despite the loss of virulence, the antigenicity and ability to produce tuberculin on suitable medium remained unaltered. In order to maintain these biochemical properties, they recommended that the BCG culture be transferred for from 2 to 3 generations on beef-bile-potato media after growing for 10 generations on bile-free media.

The ability of BCG vaccine prepared from cultures grown on bile-free media, to induce allergy, was investigated. It will be noted in table 1 that the growth of the BCG culture on bile-free media for from 2 to 7 generations was not related to the incidence of positive tuberculin reactions. In addition, the characteristics of the local reaction induced by the intracutaneous injection of vaccine preparations number 1 to 7 and 11 and to 13 inclusive were not conspicuously different. This indicates that the avirulence of the culture used in these studies was not affected by transplanting on bile-free media for a varying number of generations.

The effect of varying amounts of BCG vaccine on the local reaction has been studied by several investigators. Wallgren (4) found that the intracutaneous injection of 0.25 mg. of BCG vaccine produced suppuration of the regional lymph nodes, that the injection of 0.1 mg. caused suppuration of the nodes in but 1 of 27 children and that 25 children of this group subsequently became tuberculin-positive. He concluded, therefore, that 0.1 mg. BCG was the optimum dose for the intracutaneous route of injection. Kereszturi, Rosenberg and Park (5) found that the highest percentage of tuberculin reactions was obtained among those injected intracutaneously with 0.15 mg. BCG vaccine, while larger doses favored the production of cold abscesses without materially increasing

the incidence of tuberculin-positive cases. In this study we have injected intracutaneously either 0.1 or 0.15 mg. of BCG vaccine. The local inflammatory reaction resulting from these doses was not conspicuously different: although the immediate inflammatory reaction to the larger dose was somewhat more severe, the resulting ulcer and scar were in general comparable in character and in size to those from the smaller dose. The results of the tuberculin tests one and two years after vaccination with the different amounts of BCG vaccine are presented in table 2. Since vaccines number 8, 9 and 10 were prepared from cultures grown on veal-broth-potato, they are considered separately. It will be observed from table 2 that approximately 4 per cent more of those injected with 0.1 mg. BCG vaccine prepared from cultures grown on Sauton's medium reacted one and two years after vaccination to both doses of tuberculin than did those injected with 0.15 mg. of vaccine similarly prepared. That the injection of 0.15 mg. of the vaccine produced a higher degree of sensitivity one year after vaccination is evident, since 8 per cent more of this group reacted to the injection of 0.000,02 mg. PPD than did those injected with 0.1 mg. of the vaccine. Since a total of 93.3 per cent of those injected intracutaneously with 0.1 or 0.15 mg. BCG vaccine reacted to tuberculin one year later and since in our experience none developed suppuration of the regional lymph nodes, it would seem that either dose of vaccine may be safely used.

The relative value of vaccines prepared from cultures grown on Sauton's synthetic medium and from veal-broth-potato medium was compared, again using the tuberculin reaction as a criterion. It was found (table 1) that in those vaccinated with either preparations 1 to 7 or 11 to 13 inclusive, all prepared from cultures grown on Sauton's medium, sensitivity to tuberculin resulted one year later in from 92.6 to 100.0 per cent of cases. On the other hand, among those vaccinated with preparations 8 and 9, prepared from cultures grown on veal-broth-potato medium, 61.8 and 84.1 per cent respectively reacted to tuberculin, while the number injected with preparation number 10 was too small to be statistically significant. It will be observed (table 2) that, while the injection of 0.15 mg. of vaccine prepared from cultures grown on Sauton's medium induced allergy in 95.0 per cent of cases, the injection of a similar amount of vaccine from cultures grown on veal-broth-potato medium induced allergy in 77.4 per cent of individuals.

The greatest percentage of positive tuberculin reactions was observed among those injected with vaccines prepared from actively growing

TABLE 1

Duration of allergy and relation to different preparations of BCG vaccine

VACCINE NUMBER	AGE OF CULTURE	GENERATIONS AFTER BILE	AMOUNT INJECTED	NUMBER VACCINATED	TESTED ONE YEAR AFTER VACCINATION					TESTED TWO YEARS AFTER VACCINATION					TESTED THREE YEARS AFTER VACCINATION				
					Retested		Per cent positive to 0.000,02 mg. PPD	Per cent positive to 0.005 mg. PPD	Total per cent positive to PPD	Retested		Per cent positive to 0.000,02 mg. PPD	Per cent positive to 0.005 mg. PPD	Total per cent positive to PPD	Retested		Per cent positive to 0.000,02 mg. PPD	Per cent positive to 0.005 mg. PPD	Total per cent positive to PPD
					Number	Per cent				Number	Per cent				Number	Per cent			
1	14 days	7	0.15 mg.	88	81	92.1	48.2	44.4	92.6	72	81.8	25.0	68.1	93.1	77	87.5	48.0	40.3	88.3
2	21 days	7	0.15 mg.	169	153	90.5	61.4	33.3	94.7	143	84.6	27.9	60.9	38.8	165	97.6	36.9	57.6	94.5
3	30 days	3	0.15 mg.	101	91	90.1	59.3	36.3	95.6	96	95.0	47.9	50.0	97.9	92	91.1	53.3	44.5	97.8
4	14 days	3	0.15 mg.	115	106	92.2	39.6	59.5	99.1	110	95.6	44.5	54.6	99.1	112	97.3	51.8	48.2	100.0
5	7 days	6	0.1 mg.	12	12	100.0	33.3	66.7	100.0	12	100.0	58.3	41.7	100.0	12	100.0	50.0	50.0	100.0
6	13 days	7	0.1 mg.	170	165	95.3	41.8	56.4	98.2	162	95.3	53.1	44.4	97.5	161	94.7	36.6	57.8	94.4
7	16 days	2	0.15 mg.	97	92	94.8	13.1	80.4	93.5	95	97.9	46.3	50.5	96.8					
8*	17 days	4	0.15 mg.	127	123	96.8	13.8	48.0	61.8	120	94.5	28.3	37.5	65.8					
9*	17 days	5	0.15 mg.	164	160	97.6	15.6	72.5	88.1	154	97.6	30.5	56.5	87.0					
10*	21 days	7	0.15 mg.	10	10	100.0	50.0	50.0	100.0	10	100.0	80.0	20.0	100.0					
11	21 days	2	0.1 mg.	268	254	94.8	37.8	61.0	98.8	244	91.1	60.3	38.9	99.2					
12	19 days	3	0.1 mg.	29	28	96.6	46.4	53.6	100.0	28	96.6	75.0	25.0	100.0					
13	10 days	4	0.1 mg.	215	206	95.8	35.4	64.6	100.0	200	93.0	72.5	27.0	99.5					
Total				1,565	1,481	94.7	36.6	56.7	93.3	1,446	92.2	47.8	45.5	93.3					

* Vaccine prepared from cultures grown on veal-potato medium.
All other preparations made from cultures grown on Sauton's medium.

cultures, and while the number injected with preparation number 10 prepared from veal-broth-potato medium is small, yet it is significant that the growth in this instance was more rapid and more profuse than that present in the culture used for preparing preparations 8 and 9. The local reaction following the injection of the last two preparations was conspicuously mild. Ulceration was noted in 19.6 per cent of those injected with lot number 8 vaccine and in 44.8 per cent following lot number 9. In contrast, ulceration was noted in all cases injected with the other preparations of vaccine.

TABLE 2

The relation of the tuberculin reaction to BCG grown on various media and to dose of vaccine

AMOUNT INJECTED	NUMBER VACCINATED	RETESTED ONE YEAR AFTER VACCINATION		POSITIVE TO 0.000,02 MG. PPD		POSITIVE TO 0.005 MG. PPD		TOTAL POSITIVE		RETESTED TWO YEARS AFTER VACCINATION		POSITIVE TO 0.000,02 MG. PPD		POSITIVE TO 0.005 MG. PPD		TOTAL POSITIVE	
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
0.1 mg. (a)	694	665	95.8	255	38.3	404	60.7	659	99.0	646	93.2	406	62.8	233	36.1	639	98.9
0.15 mg. (a)	570	523	91.8	241	46.1	257	49.1	498	95.2	516	90.5	197	38.2	292	56.6	489	94.8
0.15 mg. (b)	301	293	97.3	47	16.1	180	61.4	227	77.4	284	94.5	89	31.3	134	47.2	223	78.5
Total......	1,565	1,481	94.6							1,446	92.4						

(a) Vaccine numbers 1 to 7 inclusive and 11 to 13 inclusive were prepared from cultures grown on Sauton's medium.

(b) Vaccine numbers 8 to 10 inclusive were prepared from cultures grown on veal-broth-potato medium.

DURATION OF ALLERGY

The reports dealing with the duration of allergy following the injection of BCG vaccine vary widely. Debré, Lelong and Pictet (6) found that, of 297 infants vaccinated orally and not in contact with known cases of tuberculosis, 97 per cent were tuberculin-positive during the five years of observation. Brinckmann, quoted by Kayne (7), found that, of 15 children vaccinated intracutaneously, 13 were tuberculin-negative two years later. Kayne (7) analyzed the records of over 2,000 infants vaccinated orally by Weill-Hallé. He found that the percentage of positive Pirquet reactions decreased gradually in both contact and noncontact groups. Keresztúri, Rosenberg and Park (5) observed that, one year after the intracutaneous injection of BCG, 75 per cent of their cases were tuberculin-positive, that after two years 45 per cent were positive and that after three years only 42 per cent reacted.

In the present study the persistence of the tuberculin reaction following vaccination with different preparations of BCG vaccine is shown for yearly intervals in table 1. It will be noted that, in general, the percentage of the tuberculin-positive reactors remains uniformly high during this period of observation. Among those receiving lot number 1 vaccine, 5 per cent fewer reacted to tuberculin after three years. With lot number 2 vaccine, a decrease of 6 per cent occurred two years after vaccination, while the percentage of tuberculin-positive cases three years after vaccination was the same as that noted after one year. It is possible that variations in the tuberculin reactions may be due to loss of allergy as well as to allergy resulting from a superimposed natural infection with tubercle bacilli. It is noteworthy that, despite the low antigenicity of vaccines number 8 and 9, the percentage of those who reacted to tuberculin has remained almost constant during the two years of observation. The tuberculin reactions have been compared in 1,389 cases observed for two years following vaccination. In 38.8 per cent the intensity of the reaction remained unchanged, in 39.7 per cent the reaction was more intense in character, in 21.6 per cent the degree of reaction was less marked, and in 35, or 2.5 per cent, it became doubtful or negative. Of the 35 who yielded a doubtful or negative reaction, 18 had previously been graded as two-plus or three-plus to 0.005 mg. PPD, 14 had shown a one-plus reaction to 0.005 mg. of this tuberculin, 2 a one-plus reaction to 0.000,02 mg. and one a three-plus to 0.000,02 mg.

Many investigators have used the Pirquet method for the determination of allergy after BCG vaccination. However, it is less sensitive than the intracutaneous test. Aronson, Zacks and Poutas (8) tested 4,011 persons with potent Old Tuberculin, using simultaneously the Pirquet and intracutaneous tests on each person. They found that 2.9 per cent more reacted to the intracutaneous injection of 0.01 mg. of tuberculin than to the Pirquet test and that 19 per cent of those who failed to react to the Pirquet test reacted to the injection of 1.0 mg. of tuberculin. Repetition of the Pirquet test yielded 0.8 per cent additional positive reactions. They concluded that the Pirquet test was approximately equal to the intracutaneous injection of 0.01 mg. tuberculin.

Aronson, Parr and Saylor (9) found that of 1,482 persons ranging in age from one to nineteen years, vaccinated intracutaneously one year previously with BCG vaccine, 1,383, or 93.3 per cent, reacted to the intracutaneous injection of either 0.000,02 or 0.005 mg. PPD. Of these, 39.3 per cent were positive to 0.000,02 mg. and 60.7 per cent to 0.005

mg. With the Pirquet test the 60.7 per cent would probably not have been detected.

Although the potency of the tuberculin used by different investigators is not usually stated, this information is essential in view of the marked variation in the potency of Old Tuberculin prepared by different institutions and commercial laboratories. The dose of PPD used in these studies was standardized in the initial investigations on this product against a sample of Old Tuberculin prepared by a commercial laboratory (10). Samples of this Old Tuberculin had been used extensively by Aronson (11) and by Wells and Smith (12) in epidemiological studies in the United States and in Jamaica. The potency of this preparation had been determined by the method of Lewis and Aronson (13, 14) using Old Tuberculin prepared by the United States Bureau of Animal Industry as an arbitrary standard. At the same time, one of us (JDA) determined the relative potency of a sample of the International Standard Tuberculin obtained from the Serum Institute, Copenhagen, a sample of Old Tuberculin kindly furnished us by the late Prof. W. Kolle from the Staatsinstitut für Experimentelle Therapie, Frankfurt a.M. and tuberculin prepared by the United States Bureau of Animal Industry. It was found that the Old Tuberculin prepared by the Staatsinstitut was the most potent tuberculin; the tuberculin prepared by the Bureau of Animal Industry and the tuberculin prepared by the commercial laboratory were equally potent but slightly weaker than the Frankfurt tuberculin. The International Standard tuberculin was definitely less potent than the other preparations.

DISCUSSION

The character of the local tissue response to the injection of tubercle bacilli may be indicative of the resistance of the individual to this disease. Lewis and Loomis (15) found that the injection of virulent tubercle bacilli into the skin of a strain of inbred guinea pigs resistant to tuberculosis was followed by the appearance of a sharply defined nodule. The ulcer which followed was dry, shallow and punched out and was surrounded by firm tissue. On the other hand, inbred guinea pigs from a family with little resistance to tuberculosis, when similarly infected, reacted by the formation of an ill defined lesion followed by ulceration which was more extensive, deeper, with soft oedematous margins and undermined edges. The differences in the local reaction were found to agree with the general resistance of the animals. One of us (JDA)

has made comparable observations on two different breeds of rabbits. The New Zealand red rabbit injected intracutaneously with bovine tubercle bacilli developed a sharply delimited nodule and an ulcer which tended to heal, while the Dutch breed of rabbits, similarly injected, developed a diffuse lesion and extensive ulceration. These differences in the local lesions were correlated with longevity and the extent of visceral tuberculosis.

Levine (16) found that 47.3 per cent of Negro, 41.7 per cent of Puerto Rican and 24.3 per cent of white children injected intracutaneously with 0.15 mg. of BCG vaccine developed inguinal abscesses. These lesions developed more promptly among the Negro and Puerto Rican children than among the white children. Goodwin and Schwentker (17) observed that the intramuscular injection of heat-killed tubercle bacilli induced cold abscesses in 43 per cent of the colored children and in 8 per cent of white children. Wallgren (4) noted marked variation in individual susceptibility to the intracutaneous injection of the BCG vaccine.

Similarly we have found that Indians injected intracutaneously with BCG vaccine differ widely in their local response and that these differences resemble those observed by Lewis and Loomis (15) in their inbred stock of guinea pigs. It has not been possible to correlate these variations in the lesions with differences in tribe, degree of Indian blood, sex, physical type, climate or diet.

Further observations over a period of years will be necessary to determine whether or not, in man, the local response to the injection of BCG vaccine possesses prognostic value in determining resistance to tuberculosis.

SUMMARY

1. BCG vaccine injected intracutaneously over the deltoid region of 1,565 Indians ranging in age from one to nineteen years produced no untoward local or general reactions, and in no instance was abscess formation or ulceration of the regional lymph nodes observed.

2. The local tissue response to the intracutaneous injection of BCG vaccine varied in different individuals. The relationship of the character of the local tissue reaction to resistance to tuberculosis is being studied.

3. One year after vaccination, 93.3 per cent of 1,481 persons reacted to the intracutaneous injection of either 0.000,02 or 0.005 mg. PPD.

Two years after vaccination 93.3 per cent of 1,446 who were retested were tuberculin-positive, and three years after vaccination 95.3 per cent of 619 persons reacted.

4. The antigenicity appeared to be influenced by the rate of growth of the culture used in preparing the vaccine, but was not related to the age of the culture nor to the number of generations that the culture had been grown on bile-free medium.

5. Because of marked variation in the results obtained by different investigators, it is suggested that the mode of preparation of BCG vaccine and the determination of the resulting allergy be made uniform.

6. The BCG vaccine used was prepared in a field laboratory and was used within three days. Marked differences in the colonial characteristics of the BCG culture were noted in the same flask of Sauton's medium. No evidence of progressive tuberculosis was observed in guinea pigs injected either subcutaneously or intraperitoneally with 30 mg. of the BCG culture.

REFERENCES

(1) Aronson, J. D.: Proc. Soc. Exper. Biol. & Med., 1935, *33*, 82.
(2) Calmette, A.: L'Infection bacillaire et la tuberculose, 4th ed., 1936, Paris, p. 913.
(3) Calmette, A., and Guérin, C.: Ann. Inst. Pasteur, 1924, *38*, 371.
(4) Wallgren, A.: J. A. M. A., 1928, *91*, 1876.
(5) Kereszturi, C., Rosenberg, H., and Park, W. H.: Am. Rev. Tuberc., 1937, *36*, 90.
(6) Debré, R., Lelong, M., and Pictet: Ann. Inst. Pasteur, 1932, *49*, 4.
(7) Kayne, G. G.: Am. Rev. Tuberc., 1936, *34*, 10.
(8) Aronson, J. D., Zacks, D., and Poutas, J. J.: Ibid., 1933, *27*, 465.
(9) Aronson, J. D., Parr, E. I., and Saylor, R.: Am. J. Hyg., in press.
(10) Long, E. R., Aronson, J. D., and Seibert, F.: Am. Rev. Tuberc., 1934, *30*, 733.
(11) Aronson, J. D.: Am. J. Hyg., 1931, *14*, 374; Am. Rev. Tuberc., 1933, *28*, 617; Am. J. Hyg., 1935, *21*, 543.
(12) Wells, C. W., and Smith, H. H.: Am. Rev. Tuberc., 1936, *34*, 43.
(13) Lewis, P. A., and Aronson, J. D.: Ibid., 1923, *7*, 404.
(14) Aronson, J. D.: Ibid., 1926, *13*, 263.
(15) Lewis, P. A., and Loomis, D.: J. Exper. Med., 1928, *47*, 449.
(16) Levine, M. I.: Am. J. Dis. Child., 1936, *51*, 1052.
(17) Goodwin, T. C., and Schwentker, F. F.: J. Pediat., 1934, *5*, 475.

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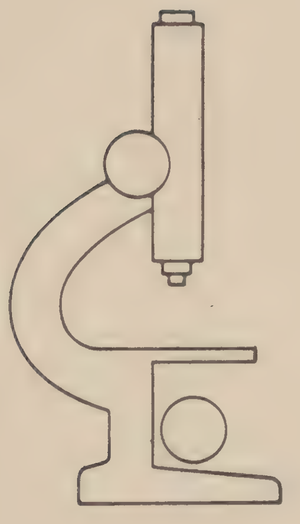

REHABILITATION

THE PROBLEM OF THE TUBERCULOUS VETERAN[1]

LOUIS I. DUBLIN[2]

The purpose of this brief paper is to bring to the attention of workers in the field of tuberculosis a situation which, strangely enough, has escaped their observation for the most part. I have in mind the failure of the Federal Government's effort to restore the tuberculous veterans of World War I to health and to economic well-being. The Government and the people certainly intended to serve the tuberculous veteran well. The chief purpose of the Veterans Administration was to rehabilitate the disabled veteran. But in spite of huge expenditures of money and of effort, the program has essentially failed. To make matters worse, this failure has constituted a menace to the general public welfare. For the large numbers of open cases of tuberculosis among veterans, under the loosest kind of supervision and control, have spread infection not only to their immediate families but to the larger circle of civilians with whom they have been in contact for longer or for shorter periods. If this pressing problem were solved, it would prove a major step in the national program for the eradication of tuberculosis.

Let us review the development of the Federal effort for veterans suffering from tuberculosis. During and immediately after the first World War, many active cases were discovered among our military personnel and veterans and their care was entrusted to the newly organized Veterans' Bureau. Many hospitals and sanatoria were erected for their treatment and this service became a major activity of the Bureau and of its successor, the Veterans Administration. As early as 1923, there were 23,653 veterans with tuberculosis admitted in a single year for treatment in veterans' hospitals or other Federal agencies. At first, care was given only to those whose disease was connected with their military service; but, subsequently, those whose disease was non-service-connected also became eligible for treatment. As a result, the number of admissions has continued large. After a quarter of a century, the annual admissions of tuberculous veterans, excluding those of the present war, still number close to 8,000. Including the new veterans, the figure for the latest fiscal year for which we have figures is nearly 10,000. For the entire period from 1919 to 1943, admissions of veterans for tuberculosis to Federal and other hospitals have exceeded 300,000. This figure represents about 200,000 different people.

No effort was spared in erecting hospitals of the latest type with excellent equipment and with as good medical personnel as could be obtained. In June, 1943, 5,671 beds were available for tuberculous patients. To meet the influx of World War II cases, additions are planned to provide a total bed capacity of

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about 7,000 by next year. The Government pays all of the costs of hospitalization and transportation and in addition pays the veterans a disability benefit. Veterans with service-connected disability resulting from active pulmonary disease receive from $70 to $100 per month, depending upon the degree of disability. Those with non-service-connected disability receive $40 per month if totally and permanently disabled. However, those without dependents receive a much smaller payment during hospitalization—$20 in service-connected cases and $8 in non-service-connected cases. For men who are treated at home, there is available an additional payment of $50 per month to the wife or other person attending the patient. In my judgment, these money benefits provide an incentive to many patients to discontinue their hospital treatment and to attempt their cure at home.

As I have indicated, the experience of the Government hospitals with tuberculous veterans has been strikingly unfavorable. Thus, in 1943, of the more than 10,000 cases discharged, only 2.3 per cent were designated arrested at discharge; and only 0.7 per cent apparently arrested. In other words, only 3 per cent of the patients discharged during the year were medically rehabilitated. The remainder of the cases were discharged either as quiescent, improved, unimproved, dead, or condition not stated. The vast majority of the patients discharged were clearly not ready to be released to civilian life. The most disturbing fact in the picture is that a large proportion of the discharged patients leave without authorization or consent. Thus, the Veterans Administration last year itself classified the hospitalization of 58 per cent of the discharged cases as incomplete.

One must admit at once that exact comparisons between various sanatoria as to results of treatment cannot be made. Nevertheless, having in mind the relatively high average age of tuberculous veterans and other adverse factors, the fact remains that the results obtained in Veterans Administration Hospitals are far inferior to those recorded year after year in well managed state, municipal and private sanatoria. This situation in the Veterans' Hospitals cannot be justified or explained away. Many sanatoria do ten times as well.

What are the reasons for this difference? The chief difficulty, in my judgment, has been the lack of appreciation on the part of Congress and of others interested in veterans' welfare, of certain fundamental conditions necessary for the effective treatment of tuberculosis. Outside pressure was brought to bear to liberalize financial provisions for these veterans. As we have seen, these provisions constitute a monetary incentive for discontinuing hospital treatment, since larger benefits are paid to many patients when they take their treatment at home. What makes matters worse is the virtual lack of control over the patients. They are not subject to the usual type of hospital restrictions. They may come and go almost at will, irrespective of their condition and against medical advice. Six to eight admissions of the same patient are a frequent occurrence in spite of attempts to control this situation. The type of discipline that is so essential for the successful treatment of the tuberculous patient is absent, for the most part, in Veterans' Hospitals. The net result of all this has been to undermine the morale of the veterans and of the doctors serving in Veterans' Hospitals.

The thousands of men who leave the Federal sanatoria before they are cured endanger the health of their families and their communities. Large numbers of them live at home, for longer or shorter periods, under little or no medical supervision. Traditionally, these tuberculous veterans have been looked upon as wards of the Federal Government and, as a result, local and state health officers have taken little responsibility for them. The patients, therefore, who fail to receive effective care from the Veterans Administration often do not receive the benefits of care in institutions operated by their own state or local governments. These men constitute an army of discouraged men who are among the important centres of tuberculous infection in their home communities.

At this late date, I question whether very much can be accomplished for World War I veterans. I am, however, genuinely disturbed over the fact that a new and large crop of tuberculous veterans is emerging from the present war. Already several thousand young veterans with tuberculosis have been admitted to Veterans' Hospitals. From present indications, there is a distinct danger that the Veterans Administration will function under the same regulations and procedures which governed the care of veterans of World War I. Evidence at hand indicates that the new veterans are showing the same restlessness and the same abandonment of regular hospital care which has produced such calamitous results among the older men. More than half of the younger veterans discharged have left against medical advice. The stage may be set for another great medical tragedy; and unless drastic action is taken, I believe that lack of discipline and mistaken generosity may not only take their toll of these young men but may also seriously delay our control of tuberculosis in the general population of the country.

We should be able to avoid such a tragedy. The present situation is far more favorable than it was during the last war and immediately thereafter. We now have at our disposal excellent medical facilities and improved skills and treatment. The new crop of tuberculous veterans is more apt to be in the early stage of the disease when the prospect for cure is usually best. There is no good reason why in many areas these young veterans should not be cared for near their own homes in state and county sanatoria which meet the proper standards for treatment of the disease. Thousands of beds are vacant and available in excellent institutions. The Veterans Administration should erect new facilities only where it is absolutely necessary to do so.

Even more important, the time is ripe for a careful revision of the basic law under which the Veterans Administration operates. The monetary incentives which have worked havoc with care of the men in tuberculosis hospitals should certainly be removed. The regulations affecting these veterans should also be changed. If the program is to be effective, tuberculous veterans must undergo hospitalization until they are restored to health or are in a safe condition to be discharged. If they will not remain in Federal hospitals, local health authorities must be promptly notified and encouraged to exercise the control over these men which the public health laws give them. Where such laws are weak, they should be strengthened. Whatever steps are necessary must be taken by health

officers to provide supervision and treatment in their own institutions for recalcitrant veterans with active tuberculosis, just as for others with the disease.

The outlook is not altogether black. The Veterans Administration and the American Legion are both aware of the seriousness of the present situation and are eager to coöperate with the state and local health officers in a well considered plan to help veterans toward rehabilitation and to protect the families of the men from infection. The American Legion is particularly anxious to help educate the men in the hospitals to take advantage of the care which is made available to them and to stay until their disease is checked. A national program has already been launched through the many local posts to further this campaign. But above and beyond all this, it is essential that a careful study be made of the operations of the Veterans' Hospitals to see on the spot the character of the service rendered in them and the conditions which must be remedied to make these institutions attractive to veterans.

Such study should cover the medical administration, the facilities for occupational therapy, the program for vocational rehabilitation and all the other elements in the program, in order to see what else may be required to help in the rehabilitation of tuberculous veterans under Federal auspices. The medical profession and the public are now sufficiently aroused to the situation regarding tuberculous veterans so that they will not be content until the Veterans' Hospitals produce results at least commensurate with the generous public provision for these institutions and which are comparable to the splendid showing of so many public and private sanatoria for the care of the tuberculous.

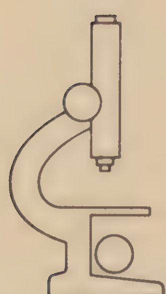
SUMMARY

Federal efforts to care for the tuberculous veterans of World War I have failed to restore these men to health and, unless radical changes are made in the present set-up and procedure, the same fate will be suffered by the tuberculous veterans of the present war.

More than 200,000 veterans of the first World War have been admitted for treatment of tuberculosis to hospitals and sanatoria operated by the Veterans Administration in the past twenty-five years. Even now approximately 7,000 such veterans of the last war are admitted each year for treatment. With few exceptions, these veterans do not get well. This is in sharp contrast with the much more favorable record over the same period for the tuberculous entering state, county and private sanatoria. This unfortunate condition arises primarily from the fact that the medical staff of the Veterans' Hospitals cannot exercise the necessary control over their patients. The good discipline essential to the care of the tuberculous is almost altogether absent in these hospitals. As a result, the physical condition of the patients deteriorates and the veteran too often goes home against medical advice where he can readily become a menace to the members of his family and to others in his community. The lack of discipline in Veterans' Hospitals is encouraged by the legislation in force which puts a financial premium on discontinuing treatment at the hospitals. Congressional legislation provided generous benefits but not the necessary safeguards. Public

interest requires that this legislation be revised to provide such safeguards in the care of tuberculous veterans as would protect these men and their families.

Because our armed forces are now three times as large as in the last war, tuberculous veterans of this war may eventually far outnumber those of the last. It would be well-nigh criminal to permit these new veterans to experience the same failure which veterans of the first World War suffered.



TUBERCULOSIS

I. Diagnosis

TUBERCULOSIS

II. Treatment